Viral Replication

1- Adsorption (Attachment): to specific Rc

2- Entry (Penetration)

3- uncoating: removal of Viral Coat by Cellular enZymes → Nucleic acid Release. (Release)

4- Eclipse 5- Assembly 6- Release.

Inclusion bodies:

- Spherical; (7 µm) Represent site of Viral Replicat

- It may be
  1- Intra Nuclear: HHV & HPV
  2- Intra Cytoplasmic: poX Virus.

Cut. Viruses

- DNA
  - intranuclear → HHVs, HPV
  - intracytoplasmic → PoX
- RNA
  - Picorna (Coxsackie) ← HFMD
  - Retroviruses: HTLV & HIV.

Coxsackie

Coxsackie

Picorna

Human Herpes Virus group.

- **Herpes:** Greek word means "To Creep or Crawl" in Reference to the spreading Nature of the dis.
- **Herpetiform:** lesion that is similar to HSV (multiple grouped vesicles on erythematous base or similar to Herpetic ulcer). [painful, superficial Erosion]

- **Human Herpes Virus group ch BY:**
  1. double stranded DNA
  2. Replicate intranuclear.
  3. **Produce:** 1ry infect → Latency → Reactivat. & Recurr. inf.
     - 1ry infect: at site of inoculat
     - Latency: in Nervous or Lymphoid Tissues.
     - Reactivat. & Recurr. inf.: in Later life either spont. or by ppt. agents

Classification of Human herpes viruses "HHVs"

HHV 1	Skin & oral mucosa → H. labialis.
HHV2	Genital areas → genital herpes.
HHV, 3	Varicella zoster.
HHV, 4	Epstein-Barr virus. → IMN & Gianotti Crosh
HHV, 5	Cytomegalovirus CMV
HHV, 6	Exanthem subitum (roseola infantum). / DRESS
HHV, 7	Associated with roseola.
HHV, 8.	Associated with KS. / Lymphoma, Multicentric Castleman's dis (Lymphoprolif. dis ch BY fever, LN, HSM)

2 Ass

	HHV	Site of latency	Manifestations	
α-HV	HHV1 (HSV1)	Nervous syst. "Neurons"	H. labialis	1° & recurrent
	HHV2 (HSV2)		Genital herpes	
	HHV3 (VZV)		Chicken pox	1°
			H. zoster	2°
β-HV	HHV5 (CMV)	Immune syst. "Lymphoid tissue"	Asympt. mono-like	
	HHV6] pit Rosea dress Synd		Roseola infantum ✓	
	HHV7]		Associated with Roseola ✓	
γ-HV	HHV4 (EBV)		Infectious mononucleosis. (IMN)	
	HHV8		KS associated herpes virus	

Herpes Simplex viruses

(HSV1 & HSV2)

- Non genital H.SV
- usually affect Non genital skin & MM.
  → Herpes labialis (Above Waist inf.)

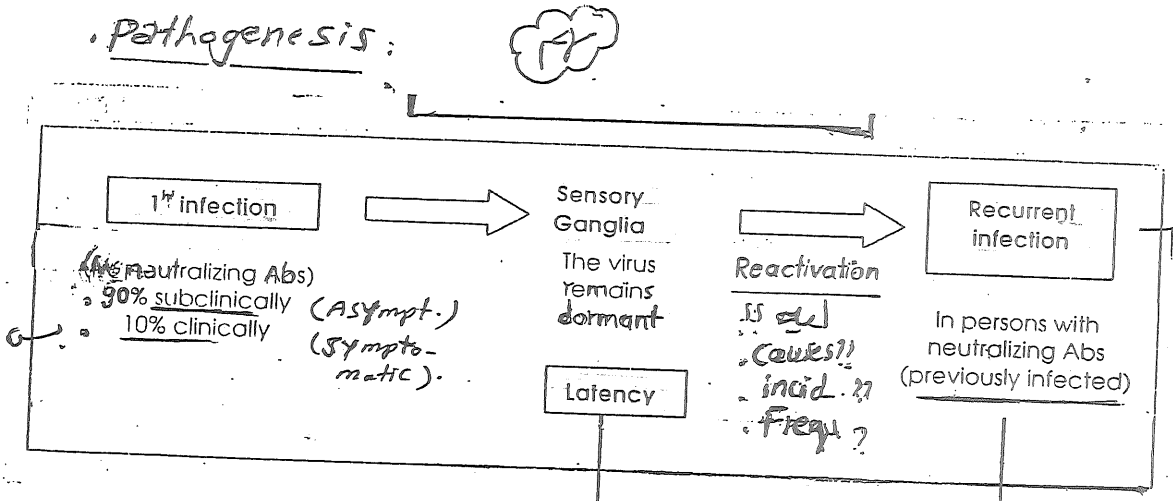
- Genital H.SV.
- usually affect Genital skin & MM.
  → Herpes Genitalis (Below Waist inf.).

NB • Nowadays HSV1 may affect the Genitalia (10-40%)
& HSV2 may affect non Genital skin & oral MM
(d.t Common practice of oral sex).
• Both produce Multiple grouped vesicles on Erythematous base at ...

• Mode of Transmission:

1. droplet inf. (in HSV1 labialis)
2. Contact with < active lesions (vesicular lesions before crusting)
   infected secretions.
3. Sexually Transmitted (HSV1 & HSV2) < oral sex
4. [placental] = Vertical Transmission (From mother → fetus)

• Pathogenesis:



- So may reinfect:
  • Face
  • Oropharyngeal MM
  • ocular MM

Site of latency
HSV1 — Trigeminal Ganglion
HSV2 — Lumbo-Sacral Ganglion (Hip, buttocks, genitalia, L.L)

Comment on:-
Types (CIP)

Types of Inf. Caused By HSV

- **Initial or first Episode Inf.**
  - **1ry** (True 1ry inf.) → Never infected by HSV1 Nor HSV2
  - **Initial Non 1ry inf.** → individual previously infected by one type & develops inf. by the other Type.
- **Recurrent inf.**
  - clinically .3 Types
    1- Symptomatic (<50%)
    2- Symptomatic unrecognized (>50%)
    3- Asymptomatic

Clinically: 10% Sympt. & 90% Asymptomatic

- **Reactivation:-**
  - Causes of reactivat:-
  - Incid.
  - No of Recurrences/y
  - C/P

(4)

(1)

- **Causes of Reactivat:** either
  1. Spontaneous
  or 2. predisp. factors: (i) [Stress, Sex, Menses] (ii) [Fatigue, Fever] (iii) [UVB (HSV1), Immuno-suppression]

Reactivat:	HSV1	HSV2
(2) Incid.	≃ 50%	≃ 90%
(3) No of Episodes	≃ 1 / Year	≃ 6 / Year

So HSV2 recurs more Common & more frequent > HSV1

Types of Recurrent inf

1. Symptomatic: classical lesions & symptoms of HSV.

2. Asymptomatic: (no S. nor S) (subclinical) the virus descends from the dorsal routes along the nerve & replicate at skin surface or MM without producing lesions or symptoms.

3. Symptomatic Unrecognized: المريض بيجيله منزمات بسيطة احمرار أو شكوى على الجلد وميش بعرف انها HSV إلا لما يروح للدكتور (non classical S & S of HSV inf.)

↓

So that periods of Transmission or shedding of the virus may occurs during:

1. Symptomatic shedding: shedding during active symptomatic lesions. ← less common period of Transmission.

2. Asymptomatic shedding: (the virus descend along the nerve → replicate without producing lesions). shedding during absence of clinical lesions.

3. Unrecognized Shedding: المريض مايعرفشي انه HSV علشان مش شكل العدوى الكلاسيكي.

(2 & 3) → the Main & The Most important Periods of Transmission.

Diseases Caused by HSV:

1. 2 main diseases
   - orolabial H-S (H. labialis or facialis)
   - Genital H-S (H. genitalis or progenitalis).

2. Other Herpetic inf:
   - ocular H-S
   - Neonatal H-S (A) — Q الامتحان
   - Herpetic Whitlow
   - Herpetic Sycosis.
   - H. Gliadialerum
   - (B) Eczema Herpeticum
   - H. Encephalitis
   - (C) Herpes in Special situations → HIV / Immuno-compromised.

NB. A, B, C → (امتحان)

Orolabial H.S (Commonest HSV inf.)

- Viral Transmission ⊙ لبراية
  - HSV1 ++
  - HSV2 ±

→ I.P: 3-7 ds.

→ Primary infection (MM) → (Herpetic Gingivo-stomatitis)

→ 10% Symptomatic
→ 90% Asymptomatic

a. Prodromal (marked) < Systemic: FAHM, L.N (tender)
Local: discomfort, burning, Tingling, Numbness & Tenderness.

b. Eruption (lesion): ⊙ presentation acc. to age:

- Vesicles
- Site
- Healing

[Gingivostomatitis: in children (<1y) → 3 sites: oral mucosa, pharynx, gingivae.
Pharyngitis: in young adults (IM like)

⊙ more numerous, Less grouped Vesicles on erythematous base → rupture → crusted (2-3 ws) → Recabit

→ Latency (in Trigeminal Ganglion)

Predisposing factors For Recurrence specially UVB (sun)

→ Reactivation

→ Recurrent episode. → (Cold sore, Fever blister)

B
Site
Vesicle
dome shapped
umbilicated.

ⓐ Prodromal ؛ as in 1ry inf. but less marked

ⓑ Eruption (lesion): - fewer No of vesicles + Marked grouping
- Healing ē in 1-2 Ws.

NB Rare Mucosal affect Except Hard palate (Hard Mucosa over Bone) & Immune Supp. (Soft mucosa)

- Site of lesions
  - Commonest lip (Vermilion border)
  - less Common
    - periotal
    - perinasal
    - cheek
    - ear lobule

(No MM affect)

(d) Recurrence: ≃ 1 / year.

- Note the difference bet. 1ry inf. & Recurrent inf.

Spec?

1ry inf.
- Prodroma
- lesions
  - No. of Vesicles
  - grouping
  - Site
  - Healing

- Note that
  - 1ry oralabial H.S : Called Herpetic Gengivo-stomatitis
  - Recurrent " " " : Called Cold Sore = Fever blister

- What is the Commonest predisposing Agents?? Sun (UVB)

1ry infection	Recurrent Infection.
- IP: 3 - 7 days	- Reactivation either spont. or under effect of certain Agents.
- usually: Children (1-5 y.) or young adults.	- Adults.
- usually: Asymptomatic (90%) & if Symptomatic it will be more severe.	- if Symptomatic → Less severe.
- Prodroma: Marked	- Less marked
- Eruption: (lesion)	
(A) - more numerous Vesicles & lesser grouping.	- Fewer Vesicles & more grouping
(B) MM: usually affected	- usually (not) affect the MM.
	lesion affect the same Region but not the exact area
(C) Healing: 2-3 Ws	- Healing 1-2 Ws

Genital Herpes

(Herpes progenitalis)

- Def. infection of Genitalia by HSV.
- AET & Transmission:
  - HSV_2 (70%) → sexual intercourse.
  - HSV_1 (30%) → oral sex.
- Types of infection:
  1- True primary inf.
  2- Initial Non primary inf.
  3- Recurrent inf.
- Periods of Transmission: ± during:
  1- symptomatic inf.
  2- Asympt. shedding
  3- sympt. unrecognized.

Most cases → 2, 3

CIP

(A) primary inf. (< 90% Asympt. / 10% Sympt)

1- IP: 2ds - 2Ws (usually 3-7ds)
2- Prodroma < local / systemic
3- lesion (Nº ∨ grouping of vesicles).

- Site
  - Rectum
    - ♂ → Homosex.
    - ♀ → ??
  - ♂ → Painful Erosive balanitis
    - Commonest at glans, shaft & rectum (in Homosex.)
    - Vesicular ulcerated lesions.
  - ♀ (Bilat).
    - Vulvitis
    - Vaginitis
    - ✓ Cervicitis (Most Common 80-90%)
    - Buttocks/perineal

- Healing: 2-3 Ws.

B- Recurrent inf.: (Reactivat.):

1- Reactivat.: cause, incid, No., Types

2- Prodroma ← local (+) / syst. (-) (Mild)

3- lesions (No & grouping of vesicles)

Site: → same Region but not the exact area (generally below Waist).

Healing: 1-2 Ws.

(H. labialis اقل)

NB 1. Recurrent inf. usually (>50٪) Asympt. or Sympt. Unrecognized.

→ 2. Initial Non 1ry inf. is more mild > True primary inf. (شديد)

Complications of H. Genitalis:

- More Common in:
  1- Women 2. 1ry inf.
- include:
  1. 2ry bact. inf. (Most common) ± → Scarring
  2. Extragenital lesions (20٪) (Cut. or Syst.)
  3. Urine Retention (15٪): d.t.
     - Lumbosacral radiculopathy
     - Reflex pain inhibition d.t intraurethral lesions.
  4. Aseptic Meningitis. (Fever, Headache, +ve Vomiting & photoph. FAHM obia).
  5. Neonatal H.S.
  6. Cancer Cervix.
  7. depression / psychosexual problems.

So Recurrent H.S of Cervix → do cytological Smear/Y.

Neonatal H.S

- Mode of Transmission:

1- Antepartum (Transplacental): (10%)

2- Intrapartum: during delivery: (90%) (via Birth Cand.)

3- Postpartum: non maternal source (kissing by infected adult) (10-15%)

(So there are 2 Sources: Maternal & non-Maternal).

- Risk of inf.

A- Episode: 1st Episode attack of mother is more dangerous > recurrent Episodes in Causing Neonatal inf. Why?? (in recurrent Episodes the fetus is protected by Maternal IgG)

- incid acc. to the Episode:

(non 1ry 1st episode) → ① True 1ry Episode → 50%

② initial non 1ry " → 30%

③ Recurrent episodes & asympt. shedding → 0-4%

B- HSV1 > HSV2 (despite its less common).

C- presence of "active lesions" at time of delivery.

D- PROM

E- Using Fetal Scalp Electrode.

NB: - The most serious is Women ⓒ 1ry inf. & having active lesion caused by HSV1 at Time of delivery. However most cases are d.t Asympt. shedding.

C/P

Ante partum (Transplacental) (10%)

- Abortion.
- IUFD.
- Prematurity.
- Cong. Anomalies:
  - Microcephaly
  - Microphthalmia
  - limb hypoplasia
  - Encephalitis
- Skin affect^: Extensive Cong. vesicles & Erosions → Healing & reticulate scarring & usually fetal

Intra partum (Commonest) (90%)

Types of affect^

1. SEM: localized inf of skin, Eye & mouth.
2. Localized CNS affect^.
3. Dissominated inf. (Multiple organs) ← CNS, Lung, Renal.
4. Non Specific Symptoms as: irritability, poor feeding & lethargy.

Complications

- Seizures
- Psychomotor retardat^.
- Spasticity
- Blindness
- learning disabilities.
- Death.

NB:
- Transplacental Transmission: has poor prognosis & High Morbidity & Mortality
- Intrapartum Transmission: has better prognosis & > 90% develops normally.

DNNZ

Eczema Herpeticum

(Kaposi Varicelliform Eruption)

HSV inf (1 or 2) + any of the following condition :

- AD.
- SD
- Scabies
- Ichyosis
- Darrier
- Hailey-Hailey (H.H)
- pemphigus.
- pemphigoid.

usually First Episode

spread of HSV throughout the diseased areas (Eczematous Areas)

- CIP : (1) IP : 5-12 ds (DNNZ)

(2) FAHM

(3) Clusters of itchy &/or painful blisters

- starts usually at head & Neck on active (or) healed site of previous skin dis (e.g AD)

7-10 ds → New patches appears at other diseased areas & may become (Generalized) 2-6 ws → + Healing (2) small white scars.

- Fever
- Severe pain
- vesicles ← Monom. umbil. fluid
- Punched out Erosion
- 2ry bact inf. & dissemind.

→ Clue for Diagnosis

- the lesion char by: monomorphic, umbilicated vesicles filled ē clear, cloudy or Hgic fluid → Hgic crust format → (painful punched out bleeding Erosions)

(4) 2ry bact. inf. may occur.

(5) in Severe Cases → systemic organ affect e.g Eyes, CNS, Lung, Liver → fatal

NB: other viruses may cause Eczema Herpeticum:

- Vaccinia virus → Eczema vaccinatum (Smallpox)
- Coxsackie ~ (A16) → ~ Coxsackium (Hand-foot & mouth dis)

NB When caused by HSV it's called Ecz. Herpeticum but when the causative virus is unknown it's called Kaposi Varicelliform Eruption

Treatment: (1) ACV or VCV: oral or IV
(2) Antibiotics
(3) Consult ophthalmologist if Eye affected

NB What is Zostriform HSV??
What is Varicelliform HZ??

chicken pox

Fluorescein ← **Ocular H-S** (Herpetic Keratoconjunctivitis)

- Keratitis, Conjunctivitis, Corneal ulcer & ± Eyelid affect
- preauricular L.N
- 2nd commonest cause of corneal blindness in USA

Specific: Trifluridin (Viroptic) : antiviral

① is it HSV_1 or HSV_2:

- if Neonatal → usually (HSV_2)
- if older than Neonate → (HSV_1)

- Pathognomonic: branching, dendritic lesions of Corneal epith.

غ الاصابع · **Herpetic whitlow** ??

· digital H-S infection occur in:

- Children : ē oral H-S
- dentists & medical personnels → HSV_1
- digital/genital Contact → HSV_2

Herpes Gladiatorum (مصارعين) ← سم الاحتكاك اثناء الالعاب الرياضية

· H-S infection occurs among Wrestlers (لاعبي المصارعة) or during practice of sports d.t close Contact.

H. Folliculis → **Herpetic Sycosis** : H-s inf. of beard & moustach of Adult → Viral Folliculitis

· Herpes infection in special situations (حالات خاصة)

A In immunocompromised: (مثل)

1- Chr. ulcerative H-S : persistent Erosions & ulcerate in Face & Perianal area.

2 Acute Generalized : (Varicella like) : wide spread Vesicular Eruption (as Varicella) → death (مرض خطير)

Verrucous Exophytic Pustular ulcerative lesion ±

3 · disseminated Visceral

4 More Frequent shedding

5 ACV Resistant H-S (مقاوم) → use (Foscarnet / Cidofavir)

B HSV + HIV : → more Severe outbreaks, More Frequent Viral shedding

· use Anti HIV + ACV (if No Resistance).

Q. How to differentiate bet. 1ry & Recurrent attacks (See prev. table H)

Q. Whole durat of dis outbreaks??
- Primary attack : 3Ws
- Recurrent " : 1w.

Q: does Frequency & Recurrence will ↓ over the time (without Tx ??) ??
- over longer periods (3-5 Ys) Frequency of outbreaks will ↓↓.

Q. Why genital Herpes is a problematic disease??

Friend of Life → because its not curable so → associated ←
social stigmata: ←
- Emotional stress
- Anger
- depression
- Guilt

→ *(So) psychological aspect should be evaluated well.

Diagnosis of HS

1. Tzanck smear:
- Rapid preliminary procedure that can be used in office
- Non specific (Can't diff. bet. HSV1 & HSV2 or even VZV)
- Results: 60-90% accurate, 3-13% False +ve.
- Method: Recently developed vesicle (<48hrs) → deroofed → Absorbant Gauze for Fluid → swabbing the base then examined by Mic or stained then examined → Multinucleated giant cells. (Toludine)

(Pathology)

(till serum obtained (# Bleeding))

2. DFA: Rapid, sensitive, diff. bet (HSV1) & (HSV2) [الأفضل والأكثر استخدام في الوقت الحالي]

3. Culture: differentiate bet. different types & Can be available within 2-5 days. (on Hela Cells)

4. PCR: good as Culture. used to detect DNA of the Virus in CSF

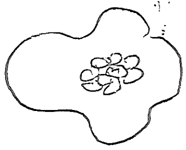
5. serology:
1. detect asympt. Carriers.
2. determine inf. Rate in Various Populat.
3. detect Couples at Risk for Neonatal H.S

- 1st general: IZA (ELISA)
- Western Blot: Very good for detect of Glycoproteins: gG1 → HSV1 & gG2 → HSV2
- WB is FDA for detect of prot-ens.

6. Histopathology : (٣٢)

أهم واحد يتعلق → ① Ballooning degen of KCs with intra-nuclear Inclusion Bodies (degenerat & Marginat of chromatin)

→ Blistering (at level of st. Spinosum.)



② Multinucleated giant Epid. Cells : (Syncytial Cells)

- Formed by fusion of infected KCs
- Nuclei are fit or molded together as pieces of puzzle. (كلها)

(NB) : Dx depends on lesional Morphology :—

- Acute Vesicular lesion —do→ Tzanck.
- Crusted, eroded or ulcerative lesion → (others)

مهم Q

- Complications of (H-SV 1) & 2 سؤال ٢٠٠٢ "خطير"

① 2ry bact. inf. ↔ scar سبب

عين ② Corneal ulcer, opacity

جسم ③ dissemination → Hepatitis, encephalitis & Pneumonia.

④ HAEM (Herpes ass. Erythema Multiform) :

H.S is the Commonest Cause of Recurrent EM

Usually after : (9) days.

أهم (٤) →

⑤ Neonatal H-S ✓

⑥ Eczema Herpeticum ✓

سؤال Pap Smear ← ⑦ Cancer Cervix. ( )

8- Complications of genital (* *)

Q Tzanck smear ?? مهم جداً كويس

Treatment of HSV inf.

Prophylactic | **Curative (active)** (Episodic ttt)
1- Topical
2- Systemic

A- For Herpes labialis (HSV1):

1. **Avoid triggers** e.g UVB —give→ sunscreen.
2. **prophylactic Antivirals** (before) — تقشير الليزر / التقشير / الأسنان
   24 hrs before (or) at morning of the procedure & for 2 Ws after that. (FCV: 250 x2 / VCV: 500 x2)

(before 4h / 2w after)

N1 → لازم اسأله إن HSV

B- For Herpes Genitalis (HSV2):

1. **Avoid sex**: (the only sure protective Method)
2. **Condom use**: prevent transmission from ♂ to ♀. (ليس العكس)
3. **Vaccine**: Glycoprotein D (HSV2) vaccine for prevention of HSV2 in women That's Sero -ve for HSV1 & HSV2 (under trial)
   (مهم: ♀ sero-ve HSV1 & 2)
   [مطلوب (Also) lupidone G & H vaccines]

C- For prevention of Neonatal HSV:

1. **Cesarean sect.** (لا نظام العد): For all cases ē active lesions or prodromal symptoms or ē pH of HSV inf.
   disadv → doesn't prevent inf. completely (d.t Transplacental)
   → Expensive.
   → ↑ Morbidity.
2. **Recently**: Measures taken if
   - the ♀ & ♂ are sero -ve
   - the ♀ sero -ve & ♂ sero +ve
   - ♀ ē Hx of recurrent HSV2

Measures for:

- **Wife:**
  - Avoid sex in last trimester
  - Vaccine (see above)
  - ACV: suppressive ## in Last Trimester (at 36 W)
- **Husband:**
  - Condom
  - ACV: suppressive ## (during last trimester)

D. Prophylactic Chr. Suppressive antiviral therapy

For recurrent inf. (HSV1 & HSV2):

- **Indications:**
  1. recurrent inf. > 6 outbreaks/y. (Herpes Associated Erythema multiforme)
  2. recurrent HAEM > ~ /y.
  3. physically or emotionally severe outbreaks.
  4. Insufficient prodrome to benifit from Episodic ##.
  5. Immuno suppression (post transplant)
  6. Suppressive ## for Sero-ve Couples.
  7. ē Kobner phenomena / ē vitilgo

- **Dose:** → see ## of H. Genitalis. (See Neonatal HSV)
- **NB:** → Resiquimod 0.01% gel is
  - Topically applied Immune response Modifier used to ↓ recurrence.

Resiquimod / Resiquimod 0.01% gel

قصه أو قصير (ـ أو ـع ـج) لمدة سنه واسبوع ←

for like أو

Active (episodic/curative) treatment of HSV infection

Topical

1. ACV 5% Cream: (Not) FDA approved
   (اخراب) دهان تحكع باعات لمدة سبع — علي → Rx to syst
2. Penciclovir 1% Cream: FDA approved
   دهان كل ساعتين أثناء عدم النوم (على الأقل ٦ مرات يوميا) لمدة ٤ أيام
3. Docosanol 10% Cream: FDA approved (lipstick)
   دهان ٥ مرات يوميا إلى أن يحدث شفاء.
4. ACV + Topical Cs → Hydrocortisone 1% → (pain) or fluocinolide 0.05%
5. Resiquimode (not a gel)

Systemic

- ✓ ACV
- ✓ VCV
- ✓ FCV

→ الجدول

أول ٤٨ ساعة بس

	Type of inf.	Treatment	
1	"Recurrent" H. labiales	• ACV: (400) → ٥ مرات يوميا لمدة ٥ أيام	5×5
	(خفيف) أيام ٣ أعراض علاج 1ry H. "labialis" ✗	• VCV: → ٢ جرام مرتين يوميا لمدة يوم	→ تشترى شريط
		• FCV: → ١.٥ جرام جرعة واحدة	→
2	• H. Genitalis	→ 1ry attack / Recurrent "	
3	• Neonatal HSV inf.	• ACV: (IV) 10 (20) mg/kg every 8 hrs for 10-21 ds (٣ مرات يوميا لمدة ٣ أسابيع)	
4	• Immunocompromised VCV 500 FCV 250	• ACV → oral: 400 X5 /d or IV: 5mg/kg/8hr (if >12ys) or 10mg/kg/8hr (if <12y) • VCV / • FCV] ٣ أقراص مرتين يوميا (durat-) "until all lesions healed"	

(NB) ACV (IV) → Neonates 10mg/kg/8hr. / Adult c̄ ↓ Imm 5mg/kg/8hr.

(IV) (5-20) → Neonates 20mg/kg/8hr / <12ys → 10mg/kg/8hr / >12y → 5mg/kg/8hr

• ACV resistent HSV inf. in Immuno-compromised eg HIV	⊙ foscarnet (IV) 40 mg/kg every 8-12 hr for 2-3 Ws (or until healing) [FDA approved] → not preferred (Nephrotoxic) • Cidofovir 1% (Cream) → [CDC approved] → (No SE) or IV Cidofovir 5mg/kg IV/W ×2Ws Then EOW.
• Chr. suppressive → in setting of NL individual / in ! setting of HIV inf.	→ See Genital H. tt & Bdiagnia.

• General Considerations:-

(A) Guide lines for Antivirals in tt of HSV

① should be given during the 1st 48hrs or during the (prodroma) (tingling, Numbness, Burning) to be effective.

② its value is: ↓ pain, ↓ shedding, ↓ Healing time.

③ Chr. suppressive tt value is:

[↓ Asymptomatic shedding by ≃ 95%
[↓ recurrence by ≃ 80-90%.

(B) Topical ACV Cream: FDA approved for limited Mucocut inf. in Immunocompromised while its use in Immunocompetent (may) be (not) effective & may cause (resistence) to systemic ACV

→ على الرغم من ذلك فكثير من الأطباء يستخدمونه

✓ (C) Penciclovir 1% & Docosanol → FDA approved for recurrent H. labialis

(D) Systemic ACV : (not) FDA approved for H. labialis but used by authors / FCV/VCV → approved.

Treatment of Herpes Genitalis

Tab:
- ACV: 400 mg
- VCV: 500
- FCV: 250

A- 1ry attack → 10 days (7-10)

- ACV (3) قرص ٣ مرات يوميًا | or 200 mg X5
- VCV (4) قرص ٤ مرات يوميا
- FCV (3) قرص ٣ مرات يوميا

B- Recurrent attack For 5 ds (5-7 d.)

- ACV → 3 (as 1ry)
- VCV → 2 tab/d — 2
- FCV → 1 tab/d — 1

C. Chr. suppressive Therapy (> 6 Recurrences/Year)

- ACV
- VCV
- FCV

} start c̄ 2 tab/d For 1 Year & Reasses For Frequency & severity.

حافظ على أقل جرعة ومنها أبتدي بعد كده

↓ تأمل → For life or Stop after 10 Ys or ACV (6 Ys) & VCV/FCV (1 Y).

طريقة أخرى له (VCV):
- < 10/Y → ١ قرص يوميا
- > 10/Y → ٢ قرص يوميا

✓ ACV oral in children:
- HSV: 15 mg/Kg (Max 400)
- Varicella Z: 20 mg/Kg (Max 800/d).

Varicella (Chicken pox)

- Def primary inf. by VZV usually effecting children.

- Etiopathogenesis

  - VZV (HHV3) ; • Double stranded DNA
    - Replicate (intra-nuclear)
    - produces primary inf. (varicella) then latency in Nerve roots reactivat → H. Zoster (2ry)

- Viral Transmission

  (1) Inhalat (main mode) of air borne droplet

  (2) Direct Contact ē infected vesicles or fluids (2ry) البس جوانتي وانا بدهنله

  (3) Vertical Transmission e.g. Transplacental

  - Viral inhalat → inf. of Conjunctiva or Mucosa of URT → replicat in regional L.N (of URT) → 1ry Viremia on days 4-6th post infect → replicat in internal organs (sp' liver, spleen) → 2ry Viremia on days 14-16 post infect → Viral invasion of epid. & capillary Endothelial cells → Cut-lesions. (4-6 days)

- Epidemiology :
  - Age : childhood (usually < 10Ys)
  - Sex : M = F.

- CIP :
  - Ip : 2-3Ws
  - Prodromal sympts : usually absent in children & may be (+ve) in adults.

• Lesion has 2 ch:

[A] Polymorphic: « all lesions are seen in all (hallmark) stages of Development ».

(Sequently progression over 12-14 hrs.)

• lesion start as: Erythematous macule → Papules → Vesicles → pustule → Crustat & → healing c̄ in (1 W) c̄out scarring

(NB) chic lesion described as: نَدى Dew drop on Rose Petal حرة البتلة

distribut = Trunk > Extremities

[B] Centripetal : starts at Face & scalp

spread: start at the Trunk → extremities (extremities to Trunk)

• oral Mucosa is often involved.

(NB) : the infectivity period: 4 (≈2) days before Erupt to [4-5 ds] after Erupt (untill all are Crusted).

٤ قبل و ٤ بعد

• Clinical varieties:

(1-) Bullous Varicella → DD (BP)

(2) Hgic Varicella [usually affect Immuncompromised]

- (Extensive) Erupt of Hgic vesicles.
- High fever & marked Constit. manifs.

• Complications of Varicella :-

(1-) 2ry bact. inf → (Scarring)
(2) Disseminated inf. → Acute encephalitis, hepatitis
(3) CNS Complication → Reye syn, Guillain Barré Syn
(4) Hgic Complications → purpura fulminans [d2 Coagulopathy]
(5) In utero VZV inf.

② Complications:-

① 2ry bact. inf. by < staph or strept → Impetigo, Cellulitis or Erysipelas → Sepsis [Life threatening].

② Disseminated 1ry Varicella:

- usually seen in → Adults & Immuno Compromised
  - CIP: → Pneumonitis (rarely ← Myocarditis, GN, Hepatitis)

③ CNS Complications: (rare)

- Reye Synd.
- Guillain-Barre synd.
- Acute Cerebellar ataxia.

④ Hgic Complications: ← Mechanism: Autoimmune

- usually affect Immuno Compromised.
- CIP:
  - Febrile purpura
  - Mg. Varicella ē purpura
  - Post infectious purpura fulminans
  - HSP.

⑤ In utero VZV inf. → Transplacental

- Maternal chicken Pox → Neonatal affect (1%) depends on Time of inf.

Period of gestation of infected mother	Outcome in the fetus
1st 2 Trimester: 7–28 weeks FVS	Fetal varicella syndrome (FVS)
1st 2 Trimester: 1–28 weeks Hz	Neonatal/childhood herpes zoster
2 weeks before delivery	Neonatal chickenpox
1 أو 3 ← 5 days before or after delivery (· 5ds before & 2ds after · 7ds & 7ds)	Neonatal disseminated chickenpox with septicemia and increased mortality (≈ 30%)

FVS: Hz: chickenpox (clinical) disseminated

(IJDVL 2010)

NB • Neonatal or Childhood HZ: occurs d.t latency of VZV of Mother in dorsal root ganglion → reactivate later on → (H-Z) (despite No History of chicken pox)

(H-Z) chicken

• Most serious Types of Neonatal affect:

IJDVL 2010 → A. Congenital (fetal) Varicella Synd (FVS):

• Etiolgy ① usually: Maternal Varicella in 1st - 2nd Trimester (sp. 13th - 20th w)

② less common (10%): d.t Maternal Zoster

• Incid: 1-2% of Maternal Varicella cases in (1st - 2nd) trimester.

• CIP:
- Cut. (70%): dermatomal scars
- Ocular (65%): Cataract, Microphthalmia, Horner Synd, Nystagmus
- Limb hypoplasia (50%):
- CNS (45%): Seizures, MR (Mental Retardation), Hydrocephalus, Cortical Atrophy
- Poor sphincter control (35%)
- Others: LBW.

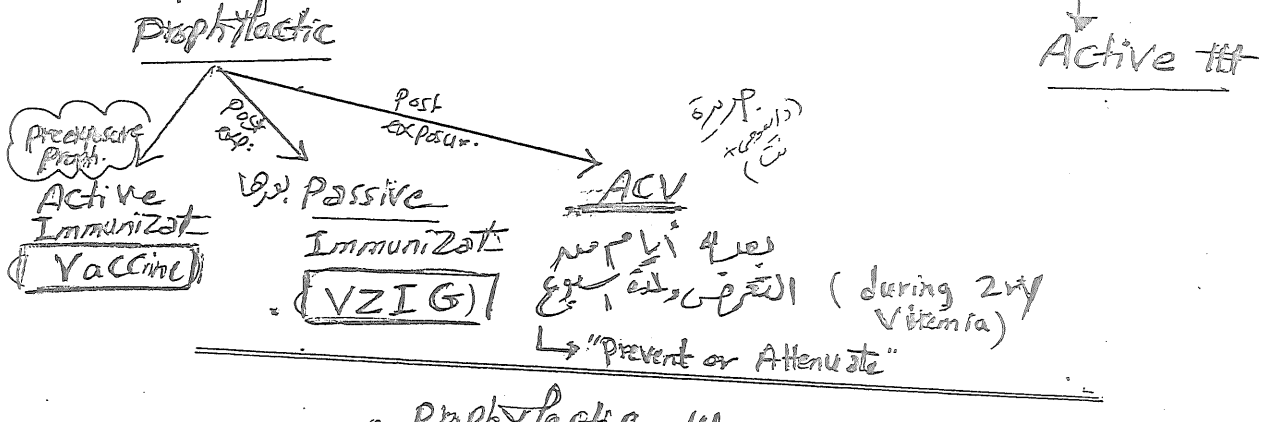
• Diagnosis:
① Amniocentesis
② fetal Blood & Chorionic Vellous sampling
[isolate of / virus or detect of ↓ IgM] specific.

DD ← Neonatal scars.

DD

- Aplasia cutis congenita ACC
- Epidermolysis bullosa (dominant dystrophic – Bart's syndrome) EBD
- Neonatal lupus erythematosus NLE
- Focal dermal hypoplasia syndrome FDHS
- Antenatal procedures – amniocentesis, forceps delivery, etc.
- Congenital erosive and vesicular dermatosis healing with supple reticulated scarring

Treatment of chicken pox



• Prophylactic tt

(A) Varicella Vaccine (USA 1995)

- live attenuated Oka strain Varicella Virus.

(Indications:)

- Healthy child (not Immuno-suppressed)
- No Past Hx. of Varicella

routine Immunizat ← 2 doses given at:

- 12-15 mos (before <12 less effective)
- 4-6 Ys.

لو مش أخدها عند هذا السن نعطيه الجرعة الثانية لغاية سن

(Catch up Immunizat of 2nd dose)

· Efficacy · (90%) → prevent inf. (100%) → protect against mod-severe inf.

· this efficacy (↓↓) ē Time (84% after 8 ys)

(✗) · NB : Break-through dis. involves Varicella that occurs after 42 ds. of Immunizat⁻ when it occurs called Modified Varicella like synd⁻ w is similar to varicella but milder & ch⁻ By :

(margin note: Recurrent Varicella)

- Milder Constit. manifs.
- NO of lesions < 50 vesicles.
- Papular lesions are common.

Passive Immunizat⁻ (VZIGs)

· Indicat⁻ :

Post exposure (in 2 situat⁻) — Neonates

· Immuno Comp.
· Mother

1. Post exposure prophylaxis: of ImmunoCompromised
2. " " " pregnant ♀
3. Neonate if ! mother acquire infect⁻ 5ds before or 5 ds after (or 2ds) delivery.

VZIG is administered intramuscularly, never intravenously. The dose is 125 U/10 kg body weight; 125 U is the minimum dose. Maximum dose is 625 IU. Administration as soon as possible after exposure is best, but VZIG can prevent or attenuate varicella if administered within 96 hours of contact. The expected duration of protection is approximately 3 weeks.

Intravenous immunoglobulin (IVIG) has been used to prevent varicella after exposure when VZIG is not available. Clinical efficacy is not exactly known. Patients already on replacement IVIG do not need VZIG if their most recent IVIG infusion was within 3 weeks.

· Efficacy: ↓ Mortality & Complications (Not) the incid.

VZIG does prevent inf. ?? Prevent or Attenuate but ↓ Mor & Complicat⁻

Active ttt

① Symptomatic ttt :

- Antihistamines
- Topical Antipruritic
- Antipyretics → ممنوع أسبرين للأطفال
- Antibiotics

↓ children ē Viral inf. (<6%) may → **Reye Synd** (Acute encephalo hepatitis)

Diagnosis: Varicella + Severe Vomiting + lost Consciousness.

② Systemic Antivirals : (ACV)

لازم خلال ٢٤ ساعة بدري (or 24-72)

varcilla → علاج ٥ أيام

H.Z → علاج ٧ أيام

Non approved Indications (Controversy)

Healthy child ≤ 12 ys (or 40 kg) ē (Un)complicated Varicella.

رأيين: ① مفيش داعي نعطيه لأنه هيخف لوحده له مضاعفات قليلة والعلاج تأثيره بسيط

② نعطيه بشرطين > المريض يقدر يدفع Cost - لو جالك أول ٢٤ ساعة

مدة علاج الـ Chicken ← ٥ أيام أو جرعة ٤ مرات

" " Zoster ← ٧ أيام أو جرعة ٥ مرات

approved Indications (لمضاعفات أكثر)

1. child > 12 ys or > 40 kg
2. child (< 12), healthy ē Complicated Varicella. (pneumonia)
3. Pregnant (oral)
4. Neonatal (IV)
5. Immuno Compromised (IV)

↓ (أو) 10 mg/Kg/8hr IV [drip over 1hr] for 7-10 ds

ACV: 20 mg/Kg/dose (max: 800 mg) ④ times/day for 5 ds.

VCV (FDA 2017 حديثاً): 20 mg/Kg/dose (max 1gm) ③ times/d for 5 ds

Herpes Zoster
(shingles)

Def: Acute condition ch. BY appearance of Grouped Vesicles along the course of a Nerve.

AET: • Reactivation of Latent VZV in dorsal Root ganglion.

- 1ry inf. by VZV → chicken pox → laten in post. Nerve Root & ganglion → Reactivation ?? → H.Z

• **Ppt. Factors:** Reactivation May occur Spontaneously but may be precipitated by certain factors:

- Immuno suppression. e.g Leuk., Lymphoma, Cs, HIV
- Drugs
- physical trauma عملية مثلاً
- stress
- Radiation

(مهمة)

- Ext. exposure to Virus. [راجل عجوز وقريبه عنده جديري أو صاحبه عنده HZ]

لو اتعرض لـ chicken pox أو HZ

Age: elderly (> 60)
Sex: M=F

clinical picture

Pain —(1-10ds) (≃ 48 hrs)→ Eruption & Manifs —(> 4 ws)→ PHN (Post Herpetic Neuralgia)

Pain:
- Called Acute Zoster pain (Prodromal pain)
- usually before eruption by (1-10ds)
- May be absent & 1st presentation is the Eruption.

Severity depend on:
- Age
- severity of eruption
- Immune Compromized.

Eruption:
- allong the affected Sensory or Motor or Cranial Nerve.
- Erythematous papules & plaques ē in hrs → Vesicles (Multiple grouped Vesicles on erythematous Base).

Pain (Prodromal & Acute Zoster pain)

- Acute Zoster غالبا نوع الألم
- "PHN" ع: الألم تقسيم نوعي هو

٣ أشكال:
- Continuous burning or dull aching — ضلوعي مكسرة
- Spasmodic shooting (Neuritic) — لسعة كهربا
- Triggered
  - Allodynia (non painful stimuli as touch → causes pain) مع لبس الهدوم
  - Hyperalgesia → (mild painful stimuli) → (severe pain)

✓ [dermatomal, unilat

- Pain before Eruption may be Misdiagnosed as: • Migraine • MI • Pleurisy • Acute Abdomen

Eruption → Commonest dermatomes: (بالترتيب)
- Thoracic
- Cervical
- Facial (cranial)
- Lumbosacral

Zoster related pain may be classified as:
1. Prodromal pain (before Erupt.)
2. Acute Zoster pain (ass. ē Erupt.)
3. PHN.

- Eruption may remain to develop over the Next 1-7 ds (ACV لازم يتعمل في الفترة دي)
- strictly unilat (Not crossing the middle lines) except in severe cases & immunocompromised)
- Healing within 2-3 ws (in healthy patients) or upto 6 ws (In immunocompromised) usually by a scar

Manifestations [Zoster mainly sensory]

1. Motor Manifestations: (5%)

[Rarely Reversable]

[Facial palsy (7th)
  ocular paralysis (5th)

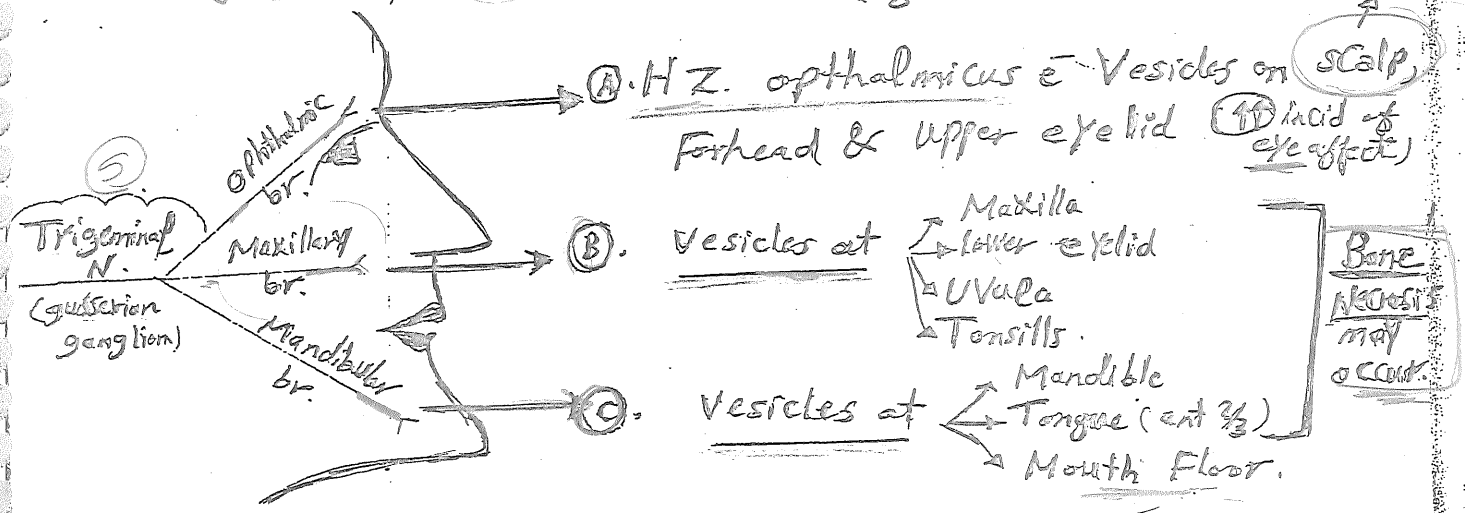
[Abd. Hernia (Tho 11) → abd. ms paralysis
  S2, 3, 4 → urine retention, hematuria, dyschezia & Pseudo obst.

2. Sensory manifs:

الأكثر

(HZO) : Hz ophthalmicus → Headache like pain (Migraine).
: N Thoracic → pleurisy or MI like pain.
: N Abd. → Acute Abdomen like.

(5) Cranial Nerve affection :- (5, 7, 8) → * Trigeminal



* (7th. Cranial (Facial Nerve)) [Reactivation of virus at Geniculate ganglion or dorsal Root]

Facial N. Paralysis is Complete & Recovery only in 2d.

(1) at First: Sensory fibers involvement (Vestigial by) → HZ Oticus
e.g. Otalgia
Vesicles at ext. auditory Canal & Pinna

(2) Pressure at Motor fibers → Ramsay Hunt Synd.
then ±

(3) Otalgia
Vesicles at Ext. auditory Canal
facial palsy (±)

(4) Pressure on 8th N. or direct Transmission of Virus (at MPA)
ear
Vertigo
dizziness
Hearing loss

(3) Pressure on Intermediate N. (or its Geniculate Ganglion) (br. from 7th.)
X loss of taste from ant 2/3 of Tongue (±)
Lacrimal gland affection.

[So, Ramsay Hunt synd is ← & usually as (e)]

NB

Eye affection in H-Z

H-Z ophthalmicus (HZO) with Vesicles on upper eyelid.

→ Ganglion of Trigem. N.

Zoster ophthalmicus Ramsay E

Eye affection by H-Z

لازم يتعمل ٣ حاجات

- IV ACV
- systemic Cs
- Ophthalmologist (in oph.) or ENT in (facial palsy)
- Consider: Meningitis.

Hutchinson's sign

Vesicles on tip & side of Nose if the ext. division of Nasociliary br. (br. from ophthalmic & supplies cornea) is involved

- When the sign ??
  - (+ve) → 75% affection
  - -ve → 25% ✓

Forms of ocular involvement:

- Uveitis (90%)
- Keratitis (50%)
- ocular paralysis.
- Irido cyclitis
- glaucoma
- Acute Retinal Necrosis.
- Argyl Robertson pubil

سؤال: مريض جه بيعد شعره وضعف [بعد ما خف] جاله H-Z ophthamicus

is "Explain" ← facial palsy & Hemiparesis

- the Trigeminal (specially ophthalmic) has intracranial branches → extension of infection from the extracranial brs. to intracranial brs → CNS affection & Cerebral arteries thrombosis → Hemi-paresis & Headache.
- (++): (systemic Antiviral)

Clinical Varieties of HZ

(سؤال مكرر)

- 3 -

1. Classical type (Vesicular)
2. Bullous (Bullae on erythematous base)
3. Abortive (Zoster sine herpete): (No) vesicles or Bullae; only pain &/or Erythema.
   (نا بيكلش) = بيروح للنيرف: neurons
4. Haemorrhagic
5. Gangrenous (Necrotic).
6. Generalized = disseminated = Zoster Varicelliform — (مهم) — > 25 extra dermatomal lesions occur 1-2 W after 1ry Eruption → [illegible] مهم
7. Ecthymatous (Punched out ulcer) — Ecthyma [illegible]
8. Verrucous

Immune-compromised = (bad prognosis) — HIV → 7, 8

مهم — Post Herpetic Neuralgia (PHN)

- <60 Y → 15%
- 60 Y → 50%
- 70 Y → 75%

] PHN

2 definitions:
- ✓ Persistence or Recurrence of pain for > 1 m from onset of Zoster (e.g. Rook)
- ✓ pain that start or persist after healing of Rash.

incidence ↑↑ in:
1. ↑ age (age > 50 is of higher Risk)
2. Immune compromised
3. Severe H.Z.
4. H.ZO or Ramsay Hunt

Rx of H.Z
- prophylactic Rx
- active Rx

• Rx of Acute Zoster
- **• Instructions**
  - ١. راحة في السرير
  - ٢. كمادات ماء (ساخن)
  - (زجاجة ماء دافئ)
  - Abd. binder
  - 3 → يوضع وتد على مكانه ويلف برباط ضاغط
- **• Topical Rx**
- **• Systemic Rx**
  - • Systemic antivirals
  - • " Cs
  - • Analgesics

• Rx of PHN
- prevention
- Active Rx
  - Topical Rx
  - Systemic Rx

Prophylaxis of Zoster

Vaccine : شرط Good Imm.

→ Live attenuated Vaccines (ZostaVax) (LAV) (Zostra Vax)

· In 2005 (For) pt. ē good Immunity.

- CDC (2006) → recommended it For any pt (≥ 60 Ys) even those ⓔ previous Zoster.
- FDA (3/2011) → (50 - 59 Ys.)

· duration of protection ??

⊙ In general indicated in:

1. Any pt > 60.
2. Any pt ≥ 60 going to have Biological therapy e.g (Ps, RA)
3. (Wiki) boosting dose may be given in pts > 60 Ys exposed to child ⓔ chicken. [Post exposure prophylaxis].

⊙ Contra indication: XX → (Immuno-Suppression. e.g Cs, chemo or radiotherapy.

Varicella-Zoster Igs

شرط : Immunocomp exposed

↓

· protect against Varicella & Zoster for (≃ 3 Ws.)

· CDC indicat. (> 60) pt. Who is susceptible or Immunocompromised & exposed to Varicella or Zoster

ويفضل الاعطاءة مبكراً بعد
التعرض للعدوى بأقصى
(الحد ٩٦ ساعة من التعرض
ممكن بين خلال)

· Value: Prevention or modification of dis.

Topical tt

Vesicular lesion

1. drying antiseptic lot
   - Burow's sol (Alum. Acetate)
   - Tr. Benzoin & Flexible Collodion (1:1)
   - Alcohol + Menthol + phenol. [Calamine]

عرض ٢ ② Acyclovir cream (٥ مرات يوميا)

Crusting lesion

Antibiotic → Topical / systemic

Systemic tt

- → Antivirals.
- → Cs.
- → analgesics.

1. Systemic Antiviral

Value:
- ↓ duration of disease course,
- ↓ pain
- ↓ incid. of PHN.
- ↓ New lesion formation.

NB: In Immunocompetent the efficacy of tt beyond 3-4ds (or 48hr) is unknown

indications:
1. All immune-compromised
2. pts > 50 ys (↑ incid of PHN)
3. HZ ophthalmicus (HZO)
4. Ramsay Hunt synd
5. severe disease or severe pain.
6. (Cut) dissiminated. visceral or Motor affection.

(NB) - Young cases c̄ mild affection → (No) need for systemic Antivi.
- the benefit of Antiviral if given (after) 3-4ds in ImmunoCompetent "unknown"
- in sever cases: we may need to start (IV)

. ACV (tab = 800) قرص ٨٠٠ مجم ٥ مرات يوميا
. VCV (tab = 500) قرص (١٠٠٠ مجم) ٣ مرات يوميا (١)
. FCV (tab = 250) مجم (٥٠٠ مجم) ٣ مرات (١/٢ م. ٣)

(7 days)

| Potency |

FCV > VCV > ACV

(لازم نبدأ خلال ٧٢ ساعة)

← نفضل بدأ العلاج في أول ٧٢ ساعة
← لكن لو كان عدى ٧٢ ساعة ولازال الطفح بيظهر جديد أو كان المريض Immunosuppressed ممكن نعطي لحد أسبوع من ظهور المرض.

- Indication of (IV) Antiviral :-
  1. immunosuppressed (ē) → ophthalmic Zoster ✓ / Ramsay Hunt Synd. ✓ / dissimination ✓
  2. Facial palsy therapy
  3. Hz ophthalmicus (HZO)

dose: 10 mg/kg/d 3 times/day for 7 ds. (IV over 1hr ??).

- in elderly patient ē unknown Renal state (2 times/d) → start ē FCV or VCV) till assessment of Renal condition

creatine clearance (HL)

- for patients ē RF (creatinine clearance of <25ml/min) → use ACV From the start

اقل الجرعة بمائة → (ACV) is prefered.

(2) Systemic Corticosteriods

فعال لـ ... Value

- ↓ pulm oedema & inflamm. → ↓ Acute Zoster Pain
- Rapid return of patient to his activity.
- ↓ Incid. of PHN (controversy)

عشان تاخدي صح

- should be with in the 1st week
- 40-60 mg/d for 1w (then) withdraw over 3-4 ws
- avoid it: in immunCompromised
- Under cover of systemic Antiviral

Mechanism: (↓) the perineural inflamm. & oedema so ↓ fibrosis.

(3) NSAIDs or opoid agonist (Tramadol).

PHN

[difficult to be prevented & treated].

(Prevention)

- Antiviral (Early ttt) → [Vcv > Acv]
- Corticosteroids (Controversy)
- Amitryptaline (25–100 mg/d)

(Tryptizol 25 tab — تعطى بالتدريج)

Amitryptaline (Tryptizole 25mg) — tabs

Treatment

Topical

- Capsicum (capsicin 0.025% & 0.075%) ®
- Lidocaine 2.5% + prilocain (EMLA) ®
- Topical Aspirine → (مسكن)
- Intralesion corticosteriods (0.2 mg/ml Intralesional or S.C]
- ① امبول كورتيكوزيت + ② امبول ميبا كيين → Intralesion Cs + Procaine
- Nerve block & Pain clinic Referral.
- ACupuncture

Systemic

سوجايات [بجد دال]

Table 2 Treatment options for postherpetic neuralgia

Drug class	Examples	Initial daily dose (mg)	Titration to maximum dose
Anticonvulsants ① ② ③ Tegretol	Gabapentin (TEN)	100–300	Start qhs and increase to tid dosing; increase by 100–300 mg every 3 days to total dose of 1800–2400 mg/day
	Pregabalin	150	Titrate up to 300 or 600 mg/day
Opioids ←	① • Tramadol		
	② Hydrocodone	5–10	No titration
	③ Oxycodone (extended-release)	20	Titrate up to 30 mg daily
Tricyclic antidepressants (TCA) ←	① Nortriptyline	10–25	Increase by 10–25 mg weekly with a target dose of 75–150 mg
	② Amitriptyline	10–25	
	③ Desipramine	10–25	

• Some authors recommend : Combination bet. Tryptizole 25mg + Tegretol 600–800 mg (Effective).
(Carbamazepin).

Antivirals Against Human Herpes Viruses

Classification

Topical

- ACV
- PCV → Penciclovir (Famciclovir)
- Docosanol
- Cidofavir → under trials
- Foscarnet → under trials

Systemic

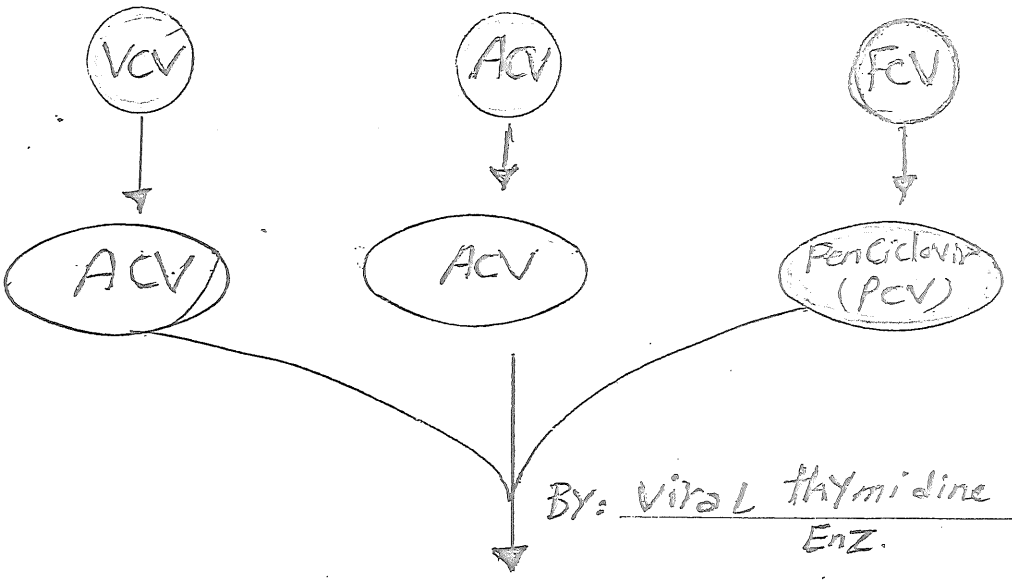
- ACV
- VCV
- FCV

Drugs:
- Cidofavir
- Foscarnet
- Ganciclovir
- Valganciclovir

- ACV (Acyclovir, Aciclovir)
- VCV (Vala ~, Vala-~)
- FCV (Fam ~, fam ~)

1- Mechanism
2- Pharmacokinetics
3. Indications
4. C.I
5. Dose
6. S.E
7. interactions.

Mechanism



By: Viral thymidine Kinase Enz.

ACV or PCV (Mono-) Phosphate

By: Cellular thymidine Kinase Enz.

ACV or PCV (Tri)phosphate

Concentrate inside infected Cells (40 times > NL Cells)

Competitive inhibition of GTP For Viral DNA Polymerase.

Stop Viral DNA Elongat=

(Chain Terminat=)

B.

VCV: Prodrug of ACV

FCV: " of PCV.

خطوات

1- Activat=: to Monophosphate form

2- Accumulat=: inside infected Cells

3- Inhibition: of DNA polymerase

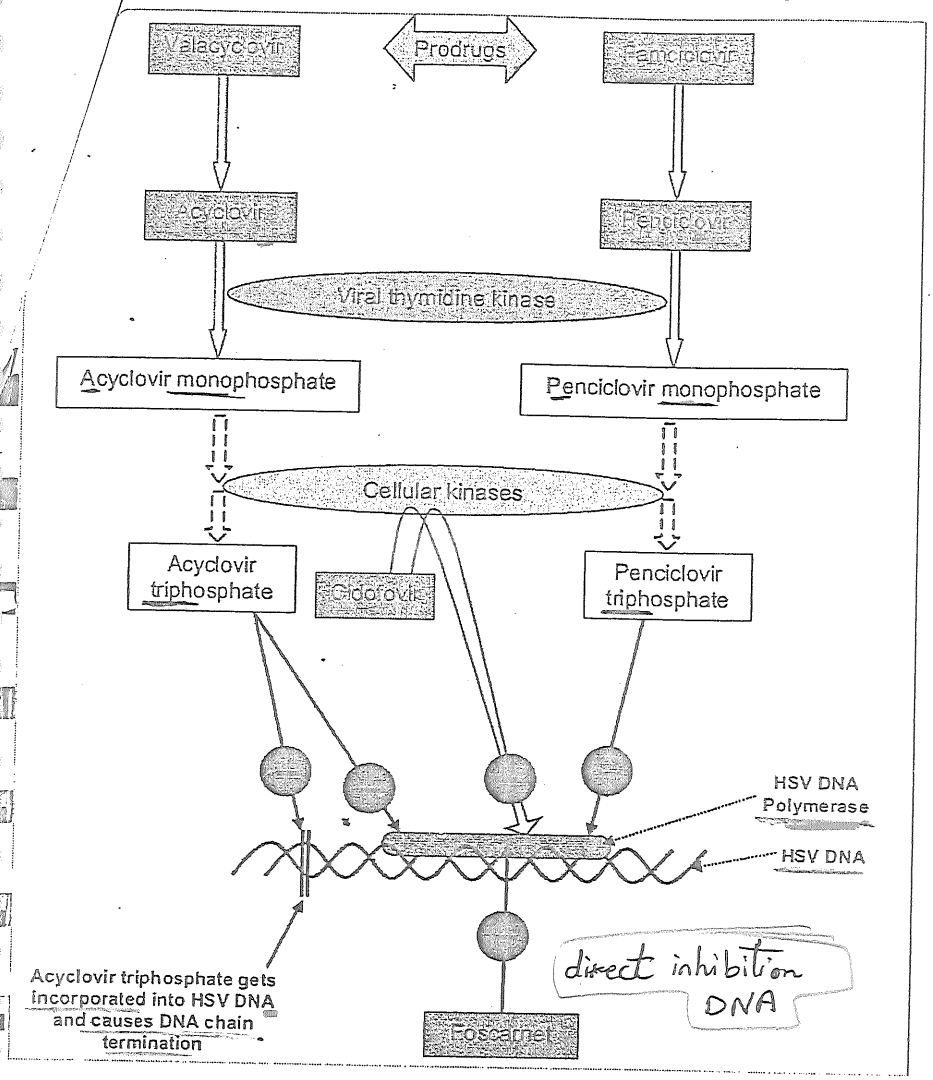
4- Chain Terminat=: -- DNA Elongat=

38

of Dermatology, and Leprology

Close

Figure 1 :Major mechanisms of action of anti-herpes simplex virus antiviral drugs



%

19

Doses : (see HSV & VZV) . يحفظ جيداً

S.E : • ACV usually safe but S.E may occurs d.t the following:

1. IV route
2. Bollous dose (if not given by IV drip over 1 hr)
3. Large doses for longer durations.

• SE may include:

عادية ٣ —
1- Headache & Cough
2- Rhinitis
3- Nausea & diarrhea.

مهم ٣ —
4- phlebitis (at site of IV)
5- Obstructive (crystalline) Nephropathy [if given rapid not By IV drip over 1hr, < 10 min] — Reversible (طبيعي)
6- Resistance. (مهم جداً)

شفوي Q: HIV مريض HZ or HS لو جاله تتعالج ازاي ؟؟

→ in (HIV) patients d.t Mutat (Fn) HSV → No viral Thymidine Kinase → No activat

↓ ايه الحل ←

Viral thymidine Kinase ?? نعطي حاجات لاتعتمد على

» Cidofovir & foscarnet » direct DNA --

↳ Cellular CK

Interactions: نادرة ليه ؟؟

↓

because it's not Metabolized by Hepatic Microsomal enzymes (CYP-450). (Cytochrome P_{450})

(احفظ كلمتين من الجدول)

Categorizat : Pregnancy Category (B)

عادي تتكتب للحامل
واحيانا لازم نظبط

Vala Cyclovir

⊙ def. L-valyl esterase of

⊙ Mechanism: V.C.V. $\xrightarrow[\text{By valacyclovir Hyd}]{\text{hepatic \& intestinal glcoring}}$ prodrug of ACV.

ACV + L-Valin

⊙ Differs from ACV in:

↑ (1) Bioavailability = (≃ 60%) (≃ 3-5 Times as ...

ACV: 50

- efficacy of oral VCV = IV ACV
- lower doses are Needed < ACV

× (2) Not approved for chicken pox (جدري الماء)

↑ (3) More effective in Ameliorating PHN > ACV.

(4) Dose: HSV → labialis → (Episodic 4 gm/d)
Genitalis → (N : 2×500×5-10)

Suppressive
- <10
- >10

HZ (500×3×7)

Famcyclovir (Famvir: 125, 250, 500) ®

very similar to VCV → but differs in:

(٣)
- Prodrug of Penciclovir.
- Bioavailability → 75%
- efficacy = VCV & ACV.

Current FDA-approved antiviral drugs (excluding antiretroviral agents)*

HSV / VZV

- Acyclovir (Zovirax®) ACV
- Famciclovir (Famvir®) FCV
- Penciclovir (Denavir®) PCV
- Foscarnet (Foscavir®)
- Valacyclovir (Valtrex®) VCV
- Trifluridine (Viroptic®)
- Vidarabine (Vira-A®)
- n-Docosanol (Abreva®)

CMV

- Ganciclovir (Cytovene®, Vitrasert®). GCV
- Valgancyclovir (Valcyte®). VGV
- Foscarnet (Foscavir®).
- Cidofovir (Vistide®).
- Fomivirsen (Vitravene®).
- HHV-8 (Kaposi's sarcoma®)
- IFN-alpha (Intron A®, Referon A®).

HPV

- IFN-alpha (Alferon N®, Intron A®).
- Imiquimod (Aldara®).

VGV

Hepatitis B virus

- IFN-alpha (Intron A®).
- Lamivudine (Epivir-HBV®).

Hepatitis C virus

- IFN-alpha (Intron-A®, Roferon-A®).
- Peg IFN-alpha (Peg Intron®).
- IFN-alpha + Ribavirin (Rebetron®).

Respiratory syncytial virus

- Rivairin (Virazole®).

Influenza virus

- Amantadine (Symmetrel®).
- Rimantadine (Flumadine®).
- Zanamivir (Relenza®).
- Oseltamivir (Tamiflu®).

* J Am Acad Dermatol. 2002. 47. 581-99.

• HPV Virology

- Papovirus Family
- Diameter: 52 - 55 µ.
- Naked; No evelop
- Capsid → 2 proteins → Major capsid Protein L1 (95%) / Minor " " (5%)
- Reservior of it → Basal KG.
- Incid: infect 10% of Populat⁻; sp. 12 - 16 Ys.
- Transmission → معروف

• Host Immune Response

"How HPV evade the Immune System"

1. No Viremia
2. low levels are expressed at KCs → Basal & st. Malpighii to be recognized by LCs & Infilt. lymphocytes.
3. Upper layers (differentiated) → Extensive Virion protein product⁻ → shedding ē epith.

• Role of Immune Surveillance ?? مراقبة

- → 60% of warts regress ē in 2 Ys.
- ↑ Incid. in pt. ē ↓CMI.
- → Antibodies against HP 16 detected in 50% of Women ē asympt. or low grade Inf.

هل هم لها علاقة ع الحد من حدوث عدوى بنفس النوع أو من الطرف الآخر (sex. Partner)

Warts (Verrucae)

- **Def** Benign Epid. proliferations (Tms) caused by Human papilloma virus (HPV) inf. of Σ skin & MM

- HPV belongs to Papovirus group ∴ are:
  - slowly growing
  - double stranded DNA ; Replicate Intranucl.
  - Naked (no envelope ; so resist drying (Freezing) Solvents)
  - > 100 types of HPVs discovered.

- Mode of Transmission:
  1. Contact: Direct e.g المصافحة باليد. / indirect e.g الملابس. / autoinoculation. (Causes → local spread.) e.g بيتحك فنفسه.
  2. Sexually transmitted.
  3. Vertical: Perinatal during vaginal delivery. أولادها قيمري

- Types of infection:
  1. clinical: Lessions seen by Gross inspection.
  2. subclinical: lesions seen only by aided exam. (acetic acid soaking).
  3. Latent: - presence of HPV virus or viral genome in apparently NL skin.
     - Thought to be common Specially in Genital Warts & Explains in part the failure of destructive methods to Eradicate Warts.

Why Recurrence is Common ←

- Epidemiology:
  - incid. of inf: 10% of children & young adults
  - Peak age incid: 12 - 16 Ys.
  - I.P: Variable ; range from 1 - 6 ms (in Common Warts)

HPV Classification

- According to Risk of Mg. Transformation
  - * Non Risky group: 1-4 types
  - * Low Risk group: 6, 11 types
  - * High Risk: usually: < 16, 18 < 31, 33, 45
- According to Type of infection → (See below)

استثناء . Verrucous SCC : HPV6 . HPV 5 & 8 : EDV	احفظ كويس جدا . 6 & 11 : Low risk. . 16, 18, 31, 33, 45 : High Risk

• HPV Infection : "مهم"

Genital

- High Risk HPV (16, 18) →
  - * Bowen's dis
  - * Bowenoid papulosis
  - * High grade intraepithelial Neoplasia.
- Low Risk HPV (6, 11) →
  - *. Genital Warts
  - *. Low grade intraepithelial Neoplasia. (IN)

⊛ Buschke & Lowenstein Tm (HPV6 استثناء)
⊙ Digital SCC (rare).

Non genital

- Cutaneous
  1. Cut warts.
  2. EDV
- Mucosal
  1. Laryngeal < Papillomatosis, Cancer
  2. Conjunctival <
  3. Oral
     - Papillomatosis
     - Cancer
     - Leukoplakia
     - Heck's dis (13, 24, 38)

NB

. كل نوع من الفيروس بيفضل مكان معين للعدوى
. عكس النوع الواحد يعمل عدوى في اماكن مختلفة

سؤال شفوي (Common ⇌ Genital)

• ↑ ~~Expression of Viral~~ ~~E6 & E7~~ & Protein E2

الاهم → (oncogenicity)

Discussion of Non genital HPV inf.

1. Cut. Warts
2. EDV
3. Heck's dis. (13, 24, 32)
4. Laryngeal papillomatosis

Cut. Warts: (Verrucae)

- Types:
  1. Common (Verruca Vulgaris)
  2. Plantar (Verrucat plantaris)
  3. Flat (Plane Wart; Verruca plana)
  4. Filiform (Digitiform)
  5. Butchers

HPV type:
- Common: 2, 4
- Mosiac: 2, 4
- Myrmecia: 1
- Cystic: 60
- Flat: 3, 10, 28
- Filiform: as Common Wart 2, 4
- Butchers: 7

أنواعه

- Description:

NB*
- Verruca lolies → Growth Rough

1. Common Wart: (Verruca Vulgaris): finger palms.
   - site: any site but
     - Commonest: Hands & Knees.
     - in Nail biters: → Lip & Tongue.
     - Butchers: on hand; caused by specific HPV ☆ is Type (7) (Not a bovine but Noted to associate butchers).
   - أجزاءه
     - extensive exophytic or Cauliflower lesions.
   - shape: Flesh colored papules → dome shapped gray to brown Hyper Keratotic discrete & Rough papules

in Nailbiters
Wart ± affect:
- periungual
- Lip & Tongue

3 NB-s

- Black Color (dots): represent thrombosed BVs.
- on paring using blade: Prominent Capillaries & ± Bleeding.
- Warts show interruption of dermatoglyphics (finger prints). XX

- prognosis: (65%) shows spont. Resolution within 2 Years.

> • All Warts are painless Except: planter wart.

HPV 2, 4

← Filiform = digitate wart: (long, slender) growths seen on (Face) around lips, eyelids & Nares.

* Flat, plane, or (Juvenile Warts): (3, 10, 28)
  - * Flat topped papules that are slightly erythematous or brown on (pale skin) & Hyperpigmented on darker skin.
  - → usually multiple
  - (Site): Face, Neck, dorsa of hands, Elbows & Knees
  - ⊙ auto inoculation: الرجال: اثناء الحلاقة / الدهر ; النساء: ازالة الشعر
  - ⊙ May show Pseudo-Koebner phenomenon (linear Flat topped papules).

(NB)

• HP of cut. warts:
1. Hyperkeratosis
2. Parakeratosis
3. Acanthosis
4. Papillomatosis
5. Vacuolization of Horny Cells
6. Koilocytosis (in EDV below granular layer)
7. Inclusion bodies
   - Basophilic: Abnl KH granules
   - Eosinophilic: Viral Particles.
8. Edematous Cell & Tortuous Capillaries

(NB) Plane wart (Not) marked Hyperk.

5

Planter Warts: 4 types

(Planter epidermoid cyst)

1. Mosiac Warts
- Plaque of closely grouped warts
- When pared: angular outline of closely compressed individual warts can be seen.
- Site: Sole (± palm)

2, 4 HPV

2. Myrmecia (Deep pp) — ترمس مكانه
Smooth, deep, dome shapped, tender (±) inflamed papule ē marked protrusion beneath the skin → Very painful

- Site: Sole & hands (digits & periungual).
  - Pressure sites: Heel & metatarsal head.

HPV 1

3. Ridged
مستديمة على الأقدام
- non weight bearing areas
- preserved skin lines (dermatoglyphics)

4. Cystic
Smooth cystic nodule on weight bearing areas
- Incision → cheesy material

HPV 60

Heck's dis. (Focal Epithelial Hyperplasia)

- HPV inf. of oral cavity: 13, 24 & 32
- Multiple flat topped (or) dome shapped "pink-white" papules affecting oral cavity (specially: lower lip). ← Q

Ttt:
- Cryo
- laser
- surgery
- IL IFN

DD: Cowden Synd.

Acrokeratotic ...

EDV

2014 (1) Epidermodysplasia Verruciformis (2014) (6)

لو جيت تاخدها جزء بيجي ٥ حاجات

1- AR (but ± sporadic, AD, sex linked)
2- HPV 5 & 8 (also other types)
3- plane wart like lesions
4- TVC like lesions
5- SCC (20-40 ys)

→ **Def** → rare inherited (AR) disorder ch. by wide spread HPV inf. & SCCs

HPV (>30) → Specific types: 5, 8 & 47 (9, 12, 14, 15, 17, 19, 25, 36-38)
→ other types (non specific): 3 & 10.

Etiopathogenesis (Triad): 1- Genetic defect: Ever 1 & EVER 2 → Immunosuppression.
2- HPV (see above)
3- UVB: Immunosuppressive & Mutagenic.

Clinically: 1 & 2 → at childhood (± cong)
3 → at Adulthood.

Plane wart like lesions
- but more extensive & Flat.
- At: Face & Neck, dorsal Hands & feet (sun exposed)

NB 3 → Plane wart like
→ Pigmented plaques
→ Dysplastic changes (AK, Bowen's, SCC).

TVC like lesions
- Scaly Hypo- or Hyper-pigm. macules

SK like plaques
- Large verrucous pink-violaceous plaq.

(TVC & SK like) → Trunk & proximal limbs.

3 SCC (UV induced)
Can affect any area of body but more common on sun exposed areas
affect 30-60% of cases bet. the age bet. 20-40 ys.

مفيش علاج
مجرد وقاية مش علاج

Rx
1. Avoid sun (to avoid SCC)
2. Surgical Rx
3. Retinoids (≠ SCC)
35 FU, Imiquimode, IFN

DD:-
1- Acrokeratosis verruciformis of Hopf:
- Infant: extensive plane wart like lesion at Hands, feet, Elbow & knee + PP Keratosis.
- HP → No vacuolization
2- Generalized verrucosis in: HIV, LL, Lymphoma

- Pathology: "specific": upper Epidermal Cells have clear, smoky or light blue cytoplasm & Central PYKnotic Nucleus, + (Hyperk + Acanthosis + Dysplasia)
  - (Clear cells) (Vacuolization)
- Insitu hybridization → detect DNA of HPV in KCs.

Recurrent Laryngeal papillomatosis

- Recurrent Respiratory (nose → lung) papillomatosis (RRP)
- may have 2 age groups:

• Age < 5

- usually acquired from the mother (during Vaginal delivery) who having Condylomata Acc.
- So the HPV is of 6 & 11 types.
- Triad of: Hoarseness, stridor, RTD
- Fatal Carcinoma.

• Age > 5

- Acquired by other Routes as plume of "smoke", Laser or Electrocautry

So → All pregnant ♀ Condylomata should undergo Cesarean sec. (despite some infants born by C.section showed laryngeal papillomatosis)

NB HPV in Immunosuppressed

- organ Transplantation
- Immunosuppressive medications
- Cong. Immunodeficiency
- Lymphoma
- HIV

→ all → defective CMI → ↑ susceptability of HPV inf.

- IncId ↑
- Type
- distribut site
- ↑ Dysplasia
- ttt ↓

CIP: ① Wide Spread: → Generalized Verrucosis (EDV like)
② ↑ Incidence of Dysplasia
③ Resistant to ttt

HIV & HPV

(i). Warty Keratoses at angles (often Bilat) chic & unique
Caused usually by HPV (2, 27 & 57.)
(ii). ↑ incid. of Genital Warts → (15 fold).
(iii). ↑ incid. of Cancer → HPV 16 & 18

D.D of Cut wart:

Callosities
1. Callus
2. Corn (clavus)
3. Black Heel
4. Pitted Keratolysis

• Callus — "non penetrating"

"diffuse" Hyperkeratotic areas

d.t chr. Repeated Friction / pressure (ill defined)

أماكن:
- Sole: under 1st & 5th metatarsal head
- Palm: الكعب
- dorsum of Hand: MCP & IPJ in bulimia individuals.
- dorsum of feet: مكان الحذاء

→ Asymptomatic or painful on pressure.

• Corn — "penetrating"

B: Conical shaped Hyperkeratotic area that's well defined

& d.t pressure, Friction or Shearing forces of bone against adjacent digits, metatarsal heads or Footwear

- Poorly fitting shoes most common cause.

غالبا بسبب حذاء ضيق

has 2 types

Hard Corn
- dorsolat aspect of fifth Toe.

وجه كلينيكال

Soft Corn
بين الإصبعين الرابع والخامس للقدم
(1 site of T. pedis)

may be d.t
- Friction of Bone of 2 Toes
- maceration

↓
- usually misdiagnosed as T. pedis.
- may produce sinus Tract in the Web → Recurrent bact. & Fungal infection.

Callus
"diffuse Hyperkeratosis"

Corn
- on the surface
- deep in skin

(Nucleus or Central Core)

"Conical Hyperkeratosis"

• رابع إصبع القدم الصغير
(dorsolat. aspect)
↓
Painful lesion
↓
Corn (usually bilat.)

بين إصبع الصغير والي قبله
↓
thickened painful area → soft corn

وقلي بالك تفرق بينه وبين الستينا

B: Pain dull discomfort or Knife like

Q: How to differentiate bet. Wart (plantar), Callus & Corn

- See Skin lines (dermatoglyphics)

- Continous over the lesion (No Central Core) → Callus

- Interrupted over the lesion with Central Nucleus (Core).
  - Wart or
  - Corn

↓ كحت بالمبرد (Paring off.)

Wart	Corn
- Markings always lost	- markings first lost over the central core but بعد continous paring → appears again.
- Bleeding	- No Bleeding. [Small toe]

I.P.F

وماتنساش الأماكن المميزة

© Treatment of Callus & Corn:

① - ﻫ of the cause: soft wears (كوتش) ↔ Correction of any bony abnormalities (Bony prominence)

② - See salicylic acid ﻫ of Wart.

③ Intra lesional Cs → dramatic Relief of pain in Corns.

" → Cancer.

"HPV of Genitalia"

Classified into:

• Low Risk or Benign types.

- ≃12 types of HPV
- Commonest: **6 & 11** (6 : 25% > 11 : 25%)

↓

مستدقة مدببة

1. **Condylomata Acuminata.** (مفرد Condyloma Accuminatum)
2. Low grade IN

• High Risk or onCogenic types

- ≃15 types of HPV.
- Commonest: **16 & 18** (also 31, 33)

↓

1. Boweneid Papulosis
2. Bowen's dis.
3. Buschke-Lowenstein Tm (استثناء سببه HPV6)
4. Intra epithelial Neoplasia → High grade
   - Vulvar IN (VIN)
   - Cervical IN (CIN)
5. → Digital Cancer

NB:
- Condyloma = knuckle.
- Acuminatum = pointed.

Condylomata Acuminata (Ano-genital Warts)

- Most Common STD among sexually active young adults in USA & Europe.
- Most infections are Latent or subclinical & this is Responsible for high incidence of Recurrence following tt.
- (أخطر ♀) Genital HPV inf. of great importance in women than men d.t Risk of Cancer Cervix.
- Genital HPV inf. closely linked to Cancer:
  - Cervix
  - glans
  - anus
  - Vulvovaginal area.
  - Periungual area. *
- Natural Hx of Genital warts:
  - Most Cases → lasting 1-2 y. then resolve.
  - Few Cases → persist.
  - Fewer " → Cancer.

⑥ other factors that ↑↑ Risk of Malignancy of HPV:

(9)

① Location of infection → Transformation Zone of Cervix, Anus (Highest Risk)
② Smoking
③ UnCircumcision (in ♂)
④ Immunosuppression
⑤ Sex ← early: before 17 y age; Multiple: 6 partners; & prostitutes.

- HPV Types: 30 types may be responsible for Genital warts & more than one type usually exist in one patient.

- Type: - HPV: 6 & 11 be (Bg or Low risk to Transformed to Mg).

- Site - may affect:

♂ → • penis, • scrotum, • anus, • intraurethral (Hematuria or Altered stream)

♀ → • Vulva, • Cervix, • anus, • perineum, • intraurethral.

- Clp: (3) clinical Varieties: according to the site:

- Acuminal Type
- Flat Type
- Common Wart like

① on dry surfaces
- Penis
- Scrotum
↓
- Hyperkeratotic Common-wart like Papules
- usually Transmitted by Contact ē Common Wart
- HPV 2, 4.

② Flat ± pigmented (SK like) Type
↓
HPV 16 ✓

③ on Moist opposed surfaces (Perianal & Perineum) (60%) = "Acuminate Type"
↓
Cauliflower mass
- pedunculated
- Flesh colored
- Verrucous
- Bleeds easily

signs of Mg
① large Protuberant mass
② Induration
③ Pain
④ Sero Sanguinous dis.

"Buschke Tm"

- NB Acummate Type & Flat ±:
- discomfort
- discharge
- Bleeding.

peroxidase

Bowenoid Papulosis (For details see Skin Cancer)

- HPV: 16 & 18
- Site: may be < Genital: Penis, Vulva & perianal.
  Extragenital: face & neck
- Clinically: Flat, (sessile), Hyperpigmented papules that difficult to be differentiated from Condyloma Acum.
- Path: Abnormal epithelial maturation & cellular atypia closely resembling Bowen's dis.
- Progression to Invasive SCC more on lesions of < Penis, Cervix, Vagina, Rectum.
- Females < with Bowenoid.
  With their husbands have Bowenoid → Risk of Cervical Dysplasia

Giant Condyloma Acuminatum of Buschke & Lowenstein

- there is a type of SCC called "Verrucous Carcinoma" it can occur in 4 sites: (all may be caused by HPV):
  (Ackerman Tm of ↓)
  1. oral cavity → Oral Florid Papillomatosis
  2. Genitalia → Buschke & Lowenstein Giant Cond.
  3. Planter aspect of foot (Sole) → Epithelioma Cuniculatum.
  4. Gottron Tm: skin
- Verrucous Carcinoma chi BY < well differentiated
  slowly growing
  Locally Mg (rarely metastasize).

Giant Condyloma Acc. of Buschke & Lowenstein:

- rare aggressive wart like growth (Fungating Condyloma like)
- Caused by HPV 6&11 (16, 18 with Carcinoma) (opposite)
- Site < Common: Glans & prepuce (of) an Circumcised ♂
  Less ♀: perianal & Vulvar.

Peroxidase

Genital warts in children

Transmission may occur

1. Vertical Transmission perinatally. (أثناء الولادة)
2. digital Autoinoculation
3. Fomites
4. Social non sexual contact.
5. Sexual Abuse. (Sign)

- Transmission acc. to age:
  - (N.B) 1st year → Vertically
  - Age > 3 Ys: → Sexual Abuse.

- Spont. Resolution often in (75%) of cases. ✓

NB annual Pap smear should be Taken From:

1. female ī genital wart (or) if Here Husband.
2. Homosexual Male ē Peri-anal Wart
3. Any genital wart in Immuno-Suppressed

D.D of Genital warts = Causes of papular / nodular Genital lesions

DD of condyloma acuminata

Sexually transmitted diseases

- Condyloma latum (syphilis): broad-based, smooth-surfaced lesion.
- Herpes simplex virus (HSV): vesicular eruption with red base and ulceration.
- Molluscum contagiosum: umbilicated yellowish papules with central core.

Common benign skin lesions

- Nevi: typically raised, but pedunculated types may occur.
- Ectopic sebaceous glands (Fordyce spots): small, yellow papules on genital and oral mucosa.
- Pearly penile papules: circumscribed papules, 1-2 mm in diameter, usually over the proximal edge of the glans penis (considered normal anatomy).

Neoplasms *(biopsy required if suspected)*

- Bowenoid papulosis: [redacted], single or multiple rough papules, 2-4 mm in diameter, flesh-colored to red-brown, recalcitrant to usual wart therapies.
- Malignant melanoma: typically single, may be flat or raised with variable color and shape.
- Giant condyloma of Buschke-Löwenstein tumor: low grade, locally invasive malignancy that can appear as a fungating condyloma.

Flat
Sessile
pigmented
Rough

"do Biopsy if there is Controversy."

Cond. Accuminata	Cond. Lata
. HPV	. T. pallidum
. Cauliflower . Flesh colored . Verrucous Surf.	. Flat . Grayish . Smooth Surf.
. Pedunculated (d.ts)	. Sessile
. bleed easily	. don't Bleed esily.

. NB : . Malignant transformation in non genital wart is Rare But may occur & so called: verrucous carcinoma that may occur on any area but commonest is plantar surface (Epethiloma Conicultum).

. A typical, non Resolving wart on hand / Periungual unit / Foot should be Biopsied to Rouled out SCC ∵ can mimic wart specially in the Region of nail unit.

Peroxidase

Diagnosis of Genital warts:

① Acetowhitening:

Aim

- a. For detection of subclinical inf. of Genitalia.
- b. detection of early lesions under foreskin.
- c. determine extent of infect. (in) patients ē multiple Recurrences.
- d. define the area Necessary For applicat° of Ttt

Method

- Acetic acid 5% (خل) applied for 5–10 mins → small macular white lesions.

False +ve

- May occur ē: Dermatitis, candida, Psoriasis. if present: Antifungal + Hydrocortisone 1% → Repeat testing after 2 ws (if +ve) → Biopsy & Histopath. Exam. For HPV.

② Histopathology: (done before Ttt of any suspicious Lesions).

3 osis
- Acanthosis (+++)
- Papillomatosis (+++)
- Koilocytosis: Cells of st. Malpighii appear ē chic
  - → Cytoplasm: Vacuolated, light-blue cytop.
  - → Nucleus: Round & Hyper-chromatic ē Perinuclear halo.

- Others (See Cut warts).

③ PCR (detect Viral DNA) [latent inf.]

④ Pap Smear For women (Even after Ttt). "مهم"

⑤ Sexual Partner Exam. For detect° of any Subclinical inf.

NB: diagnosis of:

- Subclinical inf. BY acetowhitening
- Latent inf. BY
  - PCR
  - Immuno-peroxidase

  → (detect the viral DNA inside the Nucleus)

Treatment of Cutaneous warts

* **Medical Tt**
  - Benign neglection
  - Topical
  - Intralesional
  - Systemic
  - Alternative.

* **Surgical Tt**
  - Cryosurgery
  - Electrosurgery
  - Excision Surgery
  - Lasers.

المطلوب كلمة بسيطة عن الميكانيزم
وكيفية الاستخدام.

1. Principals of Tt (أهم كونين)

① Warts or Benign cut. growths; so the Tt should be:

Benign: :!!
- no scarring
- no hazards to Patient.

[Side effects should be minimal.]

② inform the patient about (high) incid. & Recurrence Cd.t latent infection in perlesional & NLL appearing skin).

③ No specific Antiviral Tt for HPV; the Existing modalities focus primarily on → Removal or destruction
→ Immunomodulation.

④ No evidence that: Extensive Tt Results in better outcome.

⑤ with any modality: لازم العلاج يستمر فترة.
(٢-٣ شهور)
موجه للمريض

Medical Tt

1 Benign neglection:

- no Tt For warts may be carried out as this < Safe / Cost effective
why ?? because Most warts (65%) Resolve in 2 years.

but this Method may carry a risk of Transmission of autoinoculation

So indications of Ttt:

- Pain
- interference with function
- social Embarrassement
- Risk of autoinoculation
- Risk of malignancy

2. Topical Ttt

physcian's applied (5) < C, 2T, 2P — غ العيادة

a) Cantharidine 0.7% (Cantharone):
extract of blister beetles (spanish Fly) → epid. Necrosis → Blister formation.

◎ ميكانيزمه طريقة تشبه الـ Cryo

applied to wart → leave to dry & Cover For 24 hrs → (24-72 hr) blister →
Repeat Ttt after 2-3 ws.

b) Topical Immunotherapy (High Conc. 2-5%) < DNCB, SADBE, DPCP
++ immune system by induction of Contact sensitization.

c) TCA: Caustic → tissue necrosis. (50-80%)

d) Podophyllin: cytotoxic (used more ē Genital wart)

e) ALA (PDT): photosensitizer + Blue light (400-700 nm)
→ يوضع على لمسافة ٤ ساعات ثم جرعة للضوء.. مرة كل ٣ أسابيع

Patients applied (5) — في البيت

a) Keratolytics.

b) Imiquimod 5% Cream (Aldara)
- Immune Response modifier
- Used for < Genital wart (documented), Common wart (some reports)

c) Cidofovir: For Recurrent & persistent. (under trials)

d) 5-FU: Cytotoxic chemotherapeutic
- For < Flat warts (++), Common warts (+), Intraurethral (++)
- S.E. irritation & ulceration

e) Tretinoin:

NB
- TCA: يستخدم في البيت أيضا
- Topical Immunotherapy:

* Keratolytics in warts:

(a) . Mechanism <
- Mechanical: Removal of infected cells & wart virus
- induction of inflamm: → ↑↑ immunity

(b) . Commonly used: Salicylic acid (S.A):

زى بكورنيد مالكولوديان → . Paint: S.A 16.7% + Lactic acid 16.7%
. Plaster: 40% S.A.

تركيبة
- . S.A: 20%
- . Lactic: 5%
- . Base: Flexible Collodion.

(c) . Method:

(١) تنقع القدم في ماء دافئ لمدة ٥ دقائق أو أكثر
(٢) يتم حك السطح بالحجر [حجر الكعب أو المبرد]
(٣) يوضع الدهان باستخدام عود كبريت بعد احاطة الجلد السليم بفازلين ويترك ليجف
(٤) يفضل وضع بلاستر (occlusion)
(٥) تكرر العملية كل مساء مع ازالة اى تقشر بالحجر أو المبرد قبل الدهان الجديد [الاستعمال اليومى]
(٦) عند استخدام البلاستر: (40% S.A) : يوضع لفترة حتى تقل لأسبوع [ويكرر] — مهمة جدا
(٧) عند حدوث احمرار بالجلد نوقف العلاج الى ان تختفى الالتهاب — دائما استعمل

. under occlusion
. S.A 40% + TCA 50% → لفترة حوالى ٢-٣ شهور → نتيجه حوالى ٧٠-٨٠%

+ Multiple agents under occlusion

NB : . Immunotherapy
- DNCB: dinitrochloro Benzen.
- DPCP: Diphencyprone.
- SADBE: Squaric acid dibutyl ester.

. TCA: Trichloroacetate (50-80%) : (شائع التقشير - عند الطرطوب)

. ALA: Aminolevulinic acid.

. Imiquimod (بشفوى أو تحريري) 5% (Aldara®)
- . Aldara® 5% sachet
- . Zyclara® 3.75% C.

. Immune Response modifier → act on Toll like R's of Immune cells.

. exact mechanism unknown

. thought to → Cytokines Release: by KCs & virally infected cells:
- . IL1, 6 & 8, 12
- . IFN-α
- . TNF-α
- . GMCSF

→ Viral elimination.

Intralesional ⟨3⟩ (Extensive, Resistant) (19)

1. **Antigens** ⟨ Candida, Mumps - (MMR vaccine): Trichophyton, PPD (Tuberculin) → "مستشفى الصدر الباطني" , BCG

مهم 2. **Bleomycin**:

- Cytotoxic (↓ DNA synth.)
- For: recalcitrant common warts (كويسة)
- Concentration: 1 U/ml (1 mg/ml)
- For small warts (<5mm) → inject 0.1 ml
- " Large warts → " 0.2 ml

(don't exceed 1-2 ml / session) or 0.2ml-1ml / lesion.

- طريقة الحقن ⟨ Intradermal: Into & beneath the lesion
- Multiple puncture technique: توضع نقطة على السطح ثم يتم وخز السطح بالإبرة

→ till blanching → (علامة النجاح) Black crust separates into 2-4 ws [جلسة كل ٣ أسابيع]

جلسة كل ٣ أسابيع غالبا بتحتاج جلستين فقط

(128) (85) اسماء تجارية:
- Bleocin & Bleocip

الاكثر حاجة بيستخدموها بيعملوا زي ديرماجت (Anaesth → disrupt. CM → ↑ efficacy) حاجة كده زي بنج موضعي.

Minimum inj / lesion: → 0.2ml - 1ml.

Other uses (Tms).
- BCC, SCC, AK, Bowens, K's, Hemangioma.

S.E.
1. pain (use local anaesth.) (تحت سيطرة التخدير)
2. digital warts → Raynaud's phenomenon or Gangrene.
3. Cellulitis & lymphangitis
4. Patients received >14 ml → Flagellate urticaria → Chic Flagellate Hyperpigm, urticaria, Anaphylaxis.

3. **IFN-α2b**: Naturally occurring cytokine that has

- 1. anti bacterial
- 2. antiviral
- 3. anti cancer
- 4. Immunomodulatory

. Actions

مليون وحدة ٣ مرات كل اسبوع

4. **IPL & laser** ##.

↓ PDL → pulsed dye.

Systemic Tt (Immunostimulant)

1. Cimitidine: in large doses (600 mg/d) (30–40 mg/Kg/d) → immunomodulatory effect.
2. Retinoids: For extensive, Hyperkeratotic disabling Lesions in immunocompromised.
3. IV Cidofavir (under trial).
4. Zinc Sulphate (Topical (for) / oral (for)): (Some Reports): 10 mg/Kg/d (maximum 600/d) "for plantar warts".
5. Levimasole (Katex): 5 mg/Kg in 3 consecutive days / 2 ws for (5 ms).

Alternative therapy

1. Adhesio therapy: . duct tape (not Permeable & water proof)
   - Mechanism: 1. autosugg. 2. Suffocate 3. debridement
   - Good Tt specially < Children / inability to use Tt.
2. Hypnotherapy (Auto Suggestion): For Refractory warts.
3. Thermotherapy: (...)
   - Localized Heat therapy: ...
   - Water Immersion: ...
4. Garlic: Raw garlic gloves put on wart under occlusion.
5. Vaccines: (under trials).

Surgical Tt

* Cryosurgery
- Best & 1st line of Tt
- not only destroy the virus but the cells containing it.
- Freeze time: 10–30 sec. (Face / Plantar)
- No. of Cycles: 1 / Session. (2 plantar)
- No. of Session: 3 (every 1–4 w)
- Rim: 1.2 mm around the lesion.

* Electrosurgery
(Electrodissication & curettage).
- Effective but:
- S.E: pain, scar, Viral Isolation From Plume.

* Lasers
- indication: Large or Refractory lesions
- disadv: expensive & plume of.
- Type: . CO_2 laser . Nd:Yag . Pulsed dye.

* Excision-surgery
- Avoid it
- ↓
- . Scarring . Recurrence.

Treatment of Condylomata.

- Goal of Tt: Removal of exophytic lesions & Amelioration of symptoms.
- no Tt has been shown to eradicate HPV completely d.t Common Latent & subclinical infection. (So) it may be considered. (Friend of Life) (as H-SV2)

- Prevention: * Value of Condom
  - not prevent inf.
  - ++ Regression of Flat penile lesions & CIN.
  - Clearance of Couples infected ē the same HPV.

  * limiting No of Partners: remains mainstay to ↓ Transmission.

Tt

Patient applied Agent

1. Podophyllotoxin (Podofilox, Condylox)
   0.5% sol. or gel.
   دهان مرتين يوميا لمدة ٣ أيام متتالية
   ثم إيقاف ٤ أيام وتكرر الدورة لمدة ٤ دورات
   - C.I < pregnancy / area > 10 Cm²

2. Imiquimod
   Mucosal Genital wart
   (Cut. wart.)
   250 mg Sachets: → Contain 5% Cream
   Retal Suppositories: ↓
   Recurrence of Rectal Condyloma in immuno-Compromised.
   ٥ دهان مرة يوم بعد يوم لمدة ٦ أسابيع

Physician applied.

1. Cryo: Tt of Choice for pregnant
2. Podophyllin 25% in Tr. Benzoin or Collodion or Alcohol
3. TCA (80-90%): كل أسبوع (مرتين لـ ٦ أسابيع)

used for:
- Pregnant
- children.

4. Surgery: endoscopic Removal
5. Electro
6. Co2 Laser

1 million IU 3times/W For 3 WS. → [7] Intralesional interferon (Intron α2b)®

[8] 5FU.

[9] ALA (Photodynamic)

NB. on the ttt

what the difference between "تحريري"

Podophylline Resin (25%) in Tr. BenZoin (طارة الخاصة)

Crude extract of dried roots of the May apple plant.

- Contain many ingredients: the most active is Podophyllotoxin
- Used ē < Tr. Benz / Alcohol / Collodion (10-35%)
- يدهن مرة كل اسبوع ويغسل بعد حوالي ④ ساعات ويتكرر لحد اقصى ⑥ مرات
- C-I < Pregnant (Terategenic & death) (X) / area > 10 cm2 / Ulceration & Bleeding
- Less effective in dry surfaces: glans, Scrotum & labia

Podophyllotoxin 0.5%. (طارة اطفاقة)

- purified extract of Podophyllin resin (the most active ingredient in it)

So don't contain any of the ingredients responsible for toxicity of podophyllin

- More effective > Podophyllin

عشان كده نفضل عدم استخدام: Podophyllin Resin.

Imiquimod → See Mechanism اسمها تجارية

Common Wart

دهانه مرة يومياً تحت ٥- اسبوع (Cryo / SA رخيص)

Genital wart

- دهانه ٣ مرة يوم بعد يوم لمدة ⑯ أسبوع
- لبوس شرجي (↓ Recurrence)

• Imiquimod S.E:

Rare:
- mild-med. irritation
- Flaking of ps.
- Hyperpigm. (like vitiligo).
- Neuropathy

- Other indications: AK (if very scaly Cryo. 3 sessions) ; Imiq.
- EFFICACY:

Poor Penetration of non-mucosal skin so:
- Use it + S.A cr
- Cryo + Aldara & occlude.

Podophyllin < Imiquimod < Cryo < Electrocautrization

• 5 FU

1. Flat, Hyperpigmented lesion of Bowenoid.
2. Intra urethral wart.

Continous therapy
twice daily instillation of 5FU in the urethra
↓
irritation.

Intermittent therapy
twice weekly instillat° of 5FU in the urethra
↓
• NO irritation

- ممنوع البول بعد العلاج بساعة
- تجنب الجماع مع البول مع كريم الكفيه

IMIQUIMOD

- INTRODUCTION

Imiquimod (1-(2 methylpropyl)-1 H-imidazo [4, 5c] quinolin-4 amine) is an immune response modifier that stimulates innate and adaptive immune pathways, resulting in antiviral, antitumor and immunoregulatory properties

- Mechanism → Act on Toll-like Receptors 7 & (8) (TLRs 7) [expressed on surf. of ↓ lymphocytes, macrophages, dendritic cells]

↓

++ Innate Immune System

① ↑IFN-α, TNF-α, IL6, 1, 8, 12

② ++ NK Cells

③ ++ NO sec. by Macrophage.

++ Adaptive Immune System:

- Imiq + Immature APC → Mature APC → ++ Naive TC → Th1 Activat^

↓

IFN-γ

↓

① Antiviral. [viral wart ↓]

② Ant.Tm [< AK, BCC]. via <

③ Immunoreg.

④ Antiproliferative

X) Other mechanisms:

① in Keloid: ↓ VEGF, ↓ GAG, ↓ Coll.

- Imiq. → IFN → ↓mM angiogenic effect - (↓VEGF ∵ is ↑ in epid of keloid).
- Imiq. → ↓ Coll synth. & GAG synth.

② Induct. of Tm suppressor funct. via "Notch" Signaling Pathway

③ Recently: Antiproliferative & antiviral ↓↑ EGFr

- preparations.

1. Aldara®: Imiq. 5% Cream.
2. Zyclara®: " 2.5% & 3.75%

تركيزه أقل فتعتمد استعماله على مساحة أكبر لدرجة أكثر ولكنه أقل فاعلية → (Aldara < 25 Cm²)

- Indications & Methods:

FDA approved ← 2 AK, 3 Wart, 5 BCC

Non FDA (offlabel uses)

FDA approved:

① Ano-Genital Warts
Imquim. 5%
دهان ٣ مرات في الأسبوع لمدة ٤ شهور

② AK
- Aldara → دهان مرتين في الأسبوع لمدة ١٦ أسبوع
- Zyclara → دهان يوميا لمدة أسبوعين ثم راحة أسبوعين وتكرار.

BCC [non facial < 2Cm] ← شرط
Aldara
دهان عليها وحواليها ب ١سم
٥ مرات كل أسبوع لمدة ٦ شهور

Bowen

(في كل الأحوال) ← يترك الدهان لمدة ٨ ساعات (٦-١٠) ثم يشطف. [يعمل حساسية ضوئية] [فترة الليل]

- Non-FDA approved:

- Keloid → بعد الجراحة يوميا لمدة شهرين
- Common warts
- Molluscum
- SCC (insitu) → "Bowen's" (. مرة يوميا لمدة ٤ شهور)
- EMPD.
- Xeroderma pigm.
- Porokeratosis.

Adverse Effects

Topical: >10% (all at application site) Erythema (54-61%) Erosion (29-31%) Excoriation/flaking (18-25%) Edema (12-17%) Itching, burning	Systemic absorption (minimal) Headache Flu-like symptoms (fever, fatigue) Myalgia Diarrhoea

Contraindications

- Not recommended for urethral, intravaginal, cervical, rectal, or intra-anal human papilloma viral disease
- Pregnancy & Lactation :Pregnancy Category: C, Lactation: not known if distributed in breast milk; use with caution
- External Genital Warts in children: <12 years: safety and efficacy not established

Cautions

- ✓ Avoid or minimize exposure to sunlight, including sunlamps
- ✓ Do not use until skin has fully healed from any previous drug or surgical treatment
- ✓ Safety/efficacy not established for other forms of BCC besides sBCC
- ✓ Safety/efficacy not established for sBCC lesions on head, face or anogenital area
- ✓ Dosage is different for different indications
- ✓ Avoid sexual contact while cream is on skin
- ✓ Severe local inflammatory reactions of the female external genitalia can lead to severe vulvar swelling; severe vulvar swelling can lead to urinary retention; dosing should be interrupted or discontinued for severe vulvar swelling

Immunotherapy For Cut. warts

Topical — Sensitizers / IRM

(1) Sensitizers:
- DCP
- DNCB
- SADBE

(2) Antigens: BCG & Tuberculin

(3) I. Response modifier
Imiquimod.

Intralesional — Cytokines / Ag

(1) Cytokines:
- IFN α2b
- IL2

(2) Antigens:
(i) Bact.: BCG
(ii) Viral: MMR
(iii) Fungal: Candida & Dermatophyte Ag
(iv) Protein: Tuberculin & PPD.

Systemic

30-40 mg/kg/d = two tds
- Cimetidine
- Levamisole
- Zinc Sulfate

. Mechanism: ?? ± d.t ++ Th1 & -- Th2 → Th1 Cytokines profile (IL2, TNFα - IFN-γ)

MMR

. Indicat: Recalcitrant & Extensive warts.

. Dose: 0.3 ml - 0.5 ml / 2 wks till either — Clearance / 5 injects

. Methodology: Intradermal (or even S.C) at either the warts or NL skin - for

. SE (i) Local: Pain, Erythema, Induration, ulceration, Dyspigm. & Scarring

(ii) Systemic
- Flue like SES
- Anaphylaxis
- Autism (in Vaccines)
- Granulomatous Hepatitis

NB: . BCG: ++ more intense local React → Suitable for single or few warts
. MMR: effective in eradication & Both < local / distant warts.

Pox viruses

1. Molluscipox → MC
2. Parapox → orf virus, Milker Nodule virus.
3. Orthopox → Variola virus → Small pox; Vaccinia → Vaccine ef. Small pox.

Molluscum Contagiosum (MC)

- Viral skin inf. Caused by poxvirus (Molluscipox), family poxviridae.
- Etiopathogenesis:

- Virus: Cant be cultured on artificial media but on human foreskin. There are 5 types: type 1 (95%) of infections, type 2 (3%, the most common in HIV patients), types, 3, 4, and 5. No relationship between virus type and lesional morphology or anatomical distribution is known.
- Mode of transmission: contact (direct, indirect, autoinoculation), sexual transmission.
- Risky patients: children, immunocompetent adults and immunocompromised (HIV, leukemia, malignancy, sarcoidosis, atopics).

C/P

- Asymptomatic, Dome-shapped, umbilicated, pearly white, small sized papules, that's if squeezed it extrude cheesy material. Both Skin and MM can be affected.
- Clinical varieties: giant MC (Lesion ⩾ 1.5 cm), disseminated (in HIV usually facial and perioral, at eczema sites of AD), eczematous MC (type of infectious eczematoid dermatitis), inflammatory MC (inflammation, suppuration, and crustation, usually not due to 2ry infection rather than traumatic).

MC → Id / Inflamm.

DD

- Viral warts, KA, coccidioidomycosis, cryptococcosis, histoplasmosis, perforating dermatoses

Investigations

1. Dermoscopy
2. Squash prep.
3. HP.

1. Squash preparation:

microscopic examination of cellular exudate. The cellular material contained within the central umbilication may be extracted manually, flattened between 2 microscope slides, and stained. Microscopic examination of this preparation reveals the Henderson-Paterson bodies (intracytoplasmic inclusion bodies).

2. Dermoscopy: Central yellow-white lobular structure surr. by crown of Vs

2. HP: cup-shapped indentation of the epidermis into the dermis forming a crater. Within the region of the indentation, the epidermis appears thickened (acanthosis), and the cornified layer typically is disintegrated. The striking feature is the presence of intracytoplasmic, eosinophilic, granular inclusions within the keratinocytes of the basal, spinous, and granular layers of the epidermis.

These inclusions, **the Henderson-Paterson bodies**, can measure 35µm in diameter. Ultrastructural studies have shown that these bodies are membrane-bound sacs that contain numerous MC virions. The viral particles increase in size as they progress up toward the granular layer, causing compression of the nucleus to the periphery of the infected keratinocytes. The surrounding dermis is relatively unremarkable. Intact lesions show little or no inflammatory change.

HP: - as warts - also in KOH 10%

Orf (جلدي [illegible])

- Et: Orf virus (Parapox virus)
- Source, Mode & risk pts:
  - Contact ē infected animals < Sheep (غنم) / Goats , Carcasses (Sheep head / الذبيحة) , Pasture (مرعى)
  - Pts: Young-Lambs الشلاحين - ربة المنزل التي ترضع . / أطباء البيطريين و الجزارين (دوموما لحم الراس) .
  - No Transmission to Cattle or [human-to human] ضد .
- C/P: • IP: 5-6 ds.
  - Site: hands, Arms & ± face.
  - Skin lesion, ± L.N / Lymphangitis ± Fever
  - Firm, Solitary or few, red-blue papule(s) of (dorsal hand) → Hyic, Flat-topped pustule or bullae that ± show Central Crustat̄".

Firm Nodule (red-Blue) ↓ ± Hyic < Bulla or Pustule & Crustat:

- lesion ± : < Tender & Bleeds easily.

شكلها صعيد تحت الجلد وبتحس تحتها "Firm Nodule"

(Stages ≈ 6 each one lasting ≈ 1/wk)

- Stage I: Maculopapular.
- Stage 2: Targetoid lesion.
- Stage 3: Acute weeping nodule
- Stage 4: "regenerative stage": Nodule ē crustat̄ & Black dots.
- Stage 5: Papillomatous
- Stage 6: "regressive": thick crust covers the regressed lesion.

- Complications: BP / EM / Disseminated Cut. / Toxic erythema after 10-14 ds.

Inv:
- HP: pseudoepith. Hyperplasia, ulcerat̄, Necrosis, Vacuolizat̄ & disintegrat̄ of KCs., Intracytoplasmic & Intranuc. IC.
- PCR & DNA Hybridizat̄ (differentiate bet. it & Milker's Nods).

- Treatment: • Reassurance (Self limiting)
  - dressing & Antiseptic
  - Excision, Cryo, Curett For exophytic lesions.

Milker's Nodules

- as orf but differ in:
  - (1). Virus .. ??
  - (2). Transmission by: "tits of Cow".
  - (3). PCR & DNA Hybrid بنفرق بينهم

Viral Exanthema

- Viral Inf. ± associated with → Cut. Euplions (rash) → Exanthema
  Mucosal Eupl= ↘ Enanthema.
- Most Viruses produce similar rashes, so the Term "Non specific Viral Rash"

Types of Viral Exanthemata

(1) Vesicles on Erythematous base → HSV, VZV, HFMD

(2) Lacy Erythema → Erythema Infectiosum (شبكية)

(3) Diffuse Erythema → HBV, Entero & Adeno Virus. ("Scarletiniform")

(4) Acrally located papules → Gianotti Crosti (PAC)

(5) Morbilliform (Maculopapular) → Measles & G. Measels. / Erythema Infect. / Roseola Infantum. / PR.

DD of Morbilliform Rash

(1) Viral (معروفين)

(2) Drug: NSAIDs, Ampicillin, Amoxicill, INH, Thiazides.

(3) others: (rare)
- Kawasaki
- GVHD
- DRESS

طفل سخن وخدمضاد حيوي وبعدين طلعلي Rash؟؟ من الصيدلي لا الدوائي

DD: of Drug & Viral Induced Morbilliform Rash. ??

(1). Childhood Age
(2). Fever
(3). No itching
(4). Mucosal affect

→ all with Viral Exanthema > Exanthematous Drug Erupt=.

Viral Morbilliform Rash

بلاش تفاصيل
واعرف أهم
الخصائص
لكل نوع ؟؟

- Measles (Rubeola) (1st dis.)
- German Measles (Rubella)
- Erythema Infectiosum (5th dis)
- Roseola Infantum (6th dis = Exanthema Subitum)

أهم خصائص كل نوع

A. Erythema Infectiosum

- Parvovirus 19
- Slapped cheeks
- Lacy (reticulated) Erythema
- No MM affect .

B. Roseola Infantum (Exanthema Subitum)

- HHV6 & 7 .
- Age <3 (usually < 6m .. سن صغير جداً)
- Rash begins with drop of fever.
- MM → Nagayama's Spots (red papules on Soft Palate) .

. NB Parvovirus 19 also Causes
"Papular purpuric Gloves & Socks Synd."

	Measles (Rubeola)	German Measles (Rubella) Milder but serious on pregnancy.
. Virus	. Paramyxovirus (RNA)	Toga virus . (RNA)
. IP	. 2-3 ws .	1-2 ws
. Infectivity period .	. 5 ds before to 5 ds after rash	. 2 ds before & 4 ds after
. Prodroma	. Fever, Cough, Coryza, Conjunctivitis (3C) (Sn...	. Children: mild - Absent . Adult: FAHM, Nusea, ميزة Painful. occipital L.N Pain at lat. rotation of neck
. Enanthema	. Koplik's Spots: grayish-white papules at buccal mucosa at eryth. background "2ds" before & 2ds after rash.	. Forsheimers Spots: Petichae on Hard palate or Soft palate (Petichae → palat)
. Exanthema	. Maculopapular rash, starts Postauricular & at Ant. Hair lines 3ds→ Spread to all over the body 5ds→ يبدأ يختفي بترتيب	. Maculopapular rash starts & spread Caudally from face to all over the body 2-3d→ يختفي بترتيب . Rash is absent in 40%
. Complications	. OM, pneumonia . Encephalitis . . Panencephalitis (بعد ٥ سنة)	. Arthritis, Encephalitis, Thrombocytopenia & Cong. Rubella Inf. (if 1st Trimester) [Cataract, deafness, CHD, Anemia, Thrombocytopenia & Muffin baby synd) "blue Berry"
ttt	(i). Vaccinate (MMR; 12-15 ws) (ii). Supportive & Vit A	(i). Vaccine (ii) Supportive

NB1) Unilat Laterothoracic Exanth. (Asymm. periflexural Exanth. of Childhood)

- Etiology ??
- prodroma (URT & GIT) → unilat. Morbilliform or Eczematous rash that starts unilat (Axillae > Trunk > thigh) → spread to / Controlat. Sites 3-8w → spont. Resolut.

NB2) . Enteroviruses (RNA, Coxsackievirus, Echo, Feco-oral & droplet):

- HFMD & FMD
- Herpangina
- Eczema Coxsackium
- Int. organs: RT, CNS, GIT .

Hand foot & Mouth dis (2014) (HFMD)

Oral vesicular disorders caused by picornavirus (Echo- Entero V.) RNA
(i). HFMD
(ii). Herpangina
(iii). FMD

· Causative virus (Enterovirus)
- Entero → (i). Coxsackievirus A16 → most common
- (ii). Cox. A6 → severe affect: extend face, perioral, limbs, Eczema Coxsackium (vesiculobullous)
- (iii). Enterovirus (EV-71) → sepsis (neuro-complicat.)

· Mode of Transmission (
- (i) Fecal-oral route
- (ii) Contact ē infected skin lesions or oral secretions.
- (3) droplet.

· C/P: · Age < 10 y. (95% < 5 y.)
- · prodroma: FAHM, sore throat & ± diarrhea.
- · Rash: Tender / painful macules & vesicles at buccal mucosa, palate, pharynx → Hands & Feet (palms & dorsal aspects) → Erosion & ulcerat. 1w resolut.
  - on Erythematous Base.
  - Other areas (leg, buttock, genitalia)

· Other features:
1. onychomadesis
2. Neurological complicat. (ē EV-71)

· D/D (Ø is mainly clinical):
- (i) leukocytosis, lymphocytosis, ↑CRP & ESR
- (ii) Viral Isolat.: Culture, Immuno-assay & PCR (detect EV-71)

· TTT → supportive measures
- . Antipyretic
- . Analgesic
- . IV- fluid
- . Amantadine & Ribavirin ??

NB (1) one Hand & 2 Feet synd → Fungal inf.
(2) Hand-foot synd: pp. Erythema induced by chemo TTT (DNNZ)
3. Foot & Mouth dis (HFMD): serious, Epidemic, rare in human, contact ē infected "stock" 1w

Gianotti-Crosti syndrome

(PAC: Papular Acrodermatitis of childhood)

· Causative virus: (1) HBV (ayw strain), EBV, Entero (Coxsackie A16), Echovirus, RSV
- HBV, EBV & vaccine
- (2) Bact. Bartonella & Mycoplasma, strept.
- (3) Vaccinat.

Age: 2 – 6 years. (6 ms – 12 y)

Clinically
1. Non-pruritic erythematous (dull-red, flat-topped) papules (or pap. vesic.) on face, buttocks and limbs lasting about 3–8 weeks. Fading with desquamation.
   - . Extensor
   - . Buttocks
   - . Face
   - Spare:
     - . Trunk
     - . Elbow
     - . Knee
     - . PP
   - viral Exanth.
2. Enlargement of inguinal or axillary lymph nodes. (L.N), HSM, fever, ± jaundic → Severe affect. is against Ø.
3. Acute hepatitis lasting for 2 months.

.. Diagnosis: . HBS Ag.

· TTT → Conservative.

Cutaneous manifestations of hepatitis B &/or C infection (see also p. 19 in "Dermatology & Internal Medicine")
• Mixed essential cryoglobulinemia.
• Cutaneous small vessel vasculitis.
• Urticarial vasculitis.
• Porphyria cutanea tarda.
• Polyarteritis nodsa.
• Lichen planus.
• Serum sickness-like syndrome.
• Gianotti-Crosti syndrome.
• Pruritus.
• Erythema nodosum.
• Erythema multiforme.

Pityriasis rosea

(PR)

An acute, self-limiting, papulosquamous eruption with a duration of 6-8 weeks.

Pathophysiology...??

- Viral: PR has often been considered to be a viral exanthem, a view supported by the condition's seasonal occurrence, its clinical course, the possibility of epidemic occurrence, the presence of occasional prodromal symptoms, and the low rate of recurrence upper tract respiratory infections (old speaking was regarding HHV6,7, and Picronavirus...but no evidence auggested).
- Drugs : drug induced PR.

Clinical presentation: A single scaling patch (the herald patch) appears 1-10 days before the general rash. It is an oval pink or red plaque 2-5 cm in diameter, with a scale trailing just inside the edge of the lesion. The herald patch is often mistaken as ringworm. It can also be confused with psoriasis.

A few days later, more scaly patches (flat lesions) or plaques (thickened lesions) appear on the chest and back. A few may also appear on the thighs, upper arms and neck but they are uncommon on the face or scalp. These secondary lesions tend to be smaller than the herald patch. They are oval in shape with a dry surface. Like the herald patch, they may have an inner circlet of scaling. These lesions follow the relaxed skin tension lines (Langers lines) on both sides of the upper trunk so that the rash has been described as looking like a fir tree or "Christmas tree".

PR is usually asymptomatic but may be itchy . In white skin the patches are pink or red, but in darker skin they may be pigmented or they may appear white due to the scale. Postinflammatory hypo/hyperpigm. May occur.

Clinical varieties:

- Abortive PR: herald patch only, no 2ry eruptions.
- Inverted PR: affect acral areas (face, palmoplantar...DD; $).
- Localised: cervicofacial or girdle (axillae and groin).
- Generalized .
- Segmental, unilateral and Blaschkoid
- Short course (1-2ds) & persistent PR (ms-ys, often drug induced).

– Multiple Herald patches or No Herald Patch (2ry)

- Giant PR of vidal (pit.Circinata et marginata of vidal, limb-girdle PR): A morphologic variant characterized by atypical large patches that tend to be fewer in number and coalescent has been described. In this variant, commonly referred to as pityriasis circinata et marginata of Vidal or, the eruption generally appears in the axillae, the groin, or both, with the trunk and extremities usually spared.[32] Individual patches are 3-6 cm in diameter, exhibiting the characteristic central clearing and collarette of scale with surrounding erythema.

• Few
• large
• persistent
• Localized ⊕ but ± generalized
• DD. T. Circinata

- Variations in the lesions: papular, vesicular, pustular, bullous, purpuric, urticarial, EM like, lichenoid, photoexacerbated, oral, vulval and penile.

DD:

2ry syphilis: no herald patch, palmoplantar predilection, generalized LN, other manifestations, serology.

- *Pityriasiform drug eruption* (ACEI, ketotifen, bisthmus, gold, barbiturates): no herald patch, marked itching, lichenoid rash, prolonged course, postinflamm. Pigm.
- *Pityriasiform SD:* no herald patch, at midline trunk, other seborrheic areas. (greasy) & scalp, dull in color, thick scales
- *Others:* guttate Ps.& T. corporis.

NB: PR in 1st Trimester ± → Abort or premature

Treatment

1. Reassurance (مهم جداً): → self limiting.
2. Symptomatic tt: Antihistamines & Topical Cs
3. Erythromycin: 250 mg X 4 /d X 2 w (Earlier initiat → ± complete clearance)
4. NB-UVB: ↓ severity but ± → hyperpigm.
5. Systemic Cs & Dapsone: For wide spread & Eczematous PR
6. "Acv": in 1st week, 1 gm or 400 X 5 X 7

Vaccines in Dermatology

• HPV → [illegible]

TB

(1). BCG (Bacillus Calmette G.)
(2). live attenuated (LAV)

. الجرعة: أول يحقن بالجلد بعد الولادة أو بعد ذلك لو فيه خطر العدوى

. استعمالات أخرى: تحسين المناعة في حالات السل وسرطان البروستاتا

Leprosy

(1). BCG
(2). BCG + Killed M. leprae (Convit)
(3). Tawalars (M. welchii strain)
(4). Subunit Vaccine.

. يعطى لأى حد معرض للعدوى
. أو عايش في منطقة Endemic

HSV (under trial)

. Killed whole vaccine
. LAV
. Recombinant Glycosylated subunit.

أى حد معرض للعدوى .. للأزواج اللي هي sero-ve وجوزها +ve

Varicella →

طبعاً معروف..

(1). Varivax]
(2). MMR-V] LAV

. يعطى عند سن ١٢-١٥ شهر
. ويكرر عند ④-⑥ سنوات

→ prevent infection or severe attacks
→ ↓ incid. of PHN

HBV

⊙ Subunit.
⊙ Recombinant.

* 3 IM doses at: 0, 1, 6 m.

أى حد بتعامل مع دم أو معرض للعدوى زى الغسيل الكلوى

HIV (under trial)

. AIDSVAX : gp120 subunit.
. Subunit
. Recombinant

. أى حد معرض للعدوى (طبعاً معروفين)
. لسه صعب تصنيعه بس كلمتين نظرى في كتاب STDs

MMR

. LAV
. Dose: as Varicella

Acne

- "Component Vaccine"
- "Inactivated" Whole Bact.

بيشتغل ازاي

↓ IL8 & MIP2 (macrophage Inflammatory protein) Released By P. Acnes.

Melanoma

- Whole Cell Tm Vaccines
  - Autologous Tm Vaccine
  - Allogenic " "
  - Peptide Vaccines
  - Gangliaside "
- Indicate: Metastatic Melanoma

يحقن عضل أو تحت الجلد أو بالجلد

في اي Limb بيعدي لل MM

HPV Vaccine

- 3 Type ← Cervarix (2), Gardasil (4), Gardasil (9)

Cervarix (2) (16,18)	Gardasil (4) (6,11,16,18)
. No protect agnast 16,18 Genital warts	. protect . (6, 11, 16, 18)
. 0.5ml, IM : 0, 1, 6m.	. 0, 2, 6 m.
. Age approval : (♀) 10-25Y.	. ♀ : 9-26 . ♀ : 9-15
. Elderly : (♀) 26-55	. Not recommended For ♀ > 26

NB Gardasil is of 2 Types:

1. Gardasil 4 (6, 11, 16, 18)
2. Gardasil 9 (6, 11, 16, 18, 31, 33, 45, 52, 58)

(1). Type . (Purified product Major Capsid protein L1)

(2). ممنوع ممارسة الجنس لاقل من ٢٤ ساعة بعد استكمال التلقيح جرعات بعض النتيجة تمتد الى ٨ سنوات

(3). Given in Infect ??? ↔ Residual effect ∴ protect from other Strains From in the pt. doesn't Infected.

S.E

(1). local react
(2) Syncope
(3) Thrombo-embolism.

أسئلة امتحان

(A) EBV (HHV4) diseases caused by it

[1] IM = glandular fever

- Triad: Fever, L.N, Pharyn.
- Rash → Morbilliform (if given penicillin بعد ١ أسبوع) كل الى كيان
- Tonsillitis
- Hepatitis
- HSM
- Petichae (Skin, MM)
- Lymphocytosis ē Atypical lymphocytes.

[2] Others:

- Urticaria & UV
- EM & EN
- PAC & CBDC
- BCL & PLC
- Hairy leukoplakia
- Hydroa vacciniform
- Reactive genital ulcers.

Diagnosis

Anti- EBV Abs

(1). Paul Bunnel test (sheep RBCs)

(2) Monospot test (Horse RBCs).

- Hogland sign: EBV ass. ē Bilat. Eye Edema

(B) CMV

- ✓ IM like: less severe, No Tonsillitis, " Hepatitis
- ✓ In Immunocompromised: Colitis, retinitis, pneumonitis.
- ✓ Cong & Neonatal: IUGR, Jaundice, Thrombocytopenia.

(C) HHV6 & 7

- Roseola Infantum (HH6 > HHV7)
- DRESS
- PR.

(D) HHV8 امتحان

- K.S
- Lymphoma (1ry effusion)
- Multicentric Castellman dis. (Lymphoprolif. dis: Fever, L.N, HSM)

Pox Virus (5)

Type

1. Parapox : Orf virus, Conpock Virus (Bovine papular dermatitis virus).
2. orthopox : Small Pox Virus (Variola), Vaccinia, Cowpox, Monkey-pox
3. Molluscipox : MC virus
4. Yatapox.

- Vaccinia: Live virus used for Variola Vaccine.
  - C/P: ① local reaction at site; ② Eczema-Vaccinatum in AD.
- Cowpox: Cats, Cattle, Rodents.
  - Papules, Pust., eschar (Black).
- Monkey-pox: ..... Rodents.

- General ch: ∴ Double Stranded DNA
  - Small Pox & MC are Specific to Human.

نسبة إلى الرضاع

1. Orf virus (Ecthyma Contagiosum)
2. Milkers Nodules Virus (Cowpock)
3. Molluscipox (MCV)
4. Smallpox (Variola) الجدري

Orf

- Et. Orf virus (Parapox virus)
- Source, Mode & risk pts:
  - Contact ē infected animals < Sheep, Goats, Carcasses, Pasture
  - Pts: Young-Lambs
    - أطباء البيطريين والجزارين (وخصوصاً لحمة الرأس)
  - No Transmission to Cattle or human-to-human
- C/P:
  - IP: 5-6 ds.
  - Site: hands, Arms & ± face.
  - Skin lesion, ± L.N / Lymphangitis ± Fever
    - firm, solitary or few, red-blue papule(s) at dorsal hand
      - → Hyic, Flat-topped pustule or bullae that ± show Central Crust!
    - lesion ±: < Tender & Bleed, easily.

Firm Nodule (red-blue) → ± Hyic < Bulla or pustule → ± Crust!

"Firm Nodule"

Stages ≃ 6 each one lasting ≃ 1/wk

- Stage 1: Maculopapular.
- Stage 2: Targetoid lesion.
- Stage 3: Acute weeping nodule
- Stage 4: "regenerative stage"; Nodule ē Crust ± & Black dots.
- Stage 5: Papillomatous
- Stage 6: "regressive": thick Crust covers the regressed lesion.

Spontaneous recovery ē in 3-6 ws.

- Complications:
  - Scattered wide-spread Blisters.
  - Toxic Erythema after 10-14 ds.
  - EM
  - BP.

Invs:

1. HP:

- Epid. — pseudoepitheliomatous Hyperplasia; Central Necrosis & ulcerat.
- KCs: — Inclusion bodies (intracytoplasmic & Nuclear); Vacuolizat. & disaggregat. of KCs
- Dense inflam. dermal Infilt.

2. PCR: viral Identificat. in tissue Specimen

3. DNA Hybridizat.: Orf / Milker's Nodules → يعرف نفرق بينهم

Tt — تشبه ... علاج أورف

1. Reassurance (Self limiting)
2. Sympt. Tt: Moist dressings, local Antiseptics, Finger Immobilizat., Tt of 2ry bact. inf.
3. Surgical: Excision, Curettage, Electro, Cry for "Exophytic lesions".
4. Recent Tt → Cidofovir Tt. ??

Milker's Nodules

↑ animal, ↑ Ip., only IC, IB. ← زي الـ Orf بس في اختلافات

(inf. in Bovine called: Bovine papular Dermatitis)

1. Virus: Milker's nodules virus (Cow Pock virus = Para Vaccinia).
2. Transmission: From Cows (Orf = Sheeps & Goats): Direct: Cow Teats & Calf Muzzles; Indirect: Virally Contaminated objects
3. Ip: 4 ds – Several ws.
4. Inv. (i) Culture: on Bovine or Human Cells. (ii) PCR, DNA Hybridizat.
   (iii) Elect. M: of Specimen → viral particles.
   (IV) HP: "KCs": Ballooning, Spongiform Vacuolated Cells, with pale Eos. Cytoplasm; Pyknotic Nucleus + (only) Intracytoplasmic Inclusion Bodies .... late Acanthosis. / ± Necrosis.

Molluscum Contagiosum

- Viral skin inf. Caused by poxvirus (Molluscipox) , family poxviridae.
- Etiopathogenesis:

  - Virus: Cant be cultured on artificial media but on human foreskin. There are 5 types: type 1 (95%) of infections, type 2 (3%, the most common in HIV patients), types, 3, 4, and 5. No relationship between virus type and lesional morphology or anatomical distribution is known.
  - Mode of transmission: contact (direct, indirect, autoinoculation), sexual transmission.
  - Risky patients: children, immunocompetent adults and immunocompromised (HIV, leukemia, malignancy, sarcoidosis, atopics).

C/P

- Asymptomatic, Dome-shapped, umbilicated, pearly white, small sized papules, that's if squeezed it extrude cheesy material. Both Skin and MM can be affected.
- Clinical varieties: giant MC (Lesion ≥ 1.5 cm), disseminated (in HIV usually facial and perioral, at eczema sites of AD), eczematous MC (type of infectious eczematoid dermatitis), inflammatory MC (inflammation, suppuration, and crustation, usually not due to 2ry infection rather than traumatic).

DD

- Viral warts, KA, coccidioidomycosis, cryptococcosis, histoplasmosis, perforating dermatoses

Investigations

1. Squash preparation:

microscopic examination of cellular exudate. The cellular material contained within the central umbilication may be extracted manually, flattened between 2 microscope slides, and stained. Microscopic examination of this preparation reveals the Henderson-Paterson bodies (intracytoplasmic inclusion bodies).

2. HP: cup-shapped indentation of the epidermis into the dermis forming a crater. Within the region of the indentation, the epidermis appears thickened (acanthosis), and the cornified layer typically is disintegrated. The striking feature is the presence of intracytoplasmic, eosinophilic, granular inclusions within the keratinocytes of the basal, spinous, and granular layers of the epidermis.

These inclusions, **the Henderson-Paterson bodies**, can measure 35µm in diameter. Ultrastructural studies have shown that these bodies are membrane-bound sacs that contain numerous MC virions. The viral particles increase in size as they progress up toward the granular layer, causing compression of the nucleus to the periphery of the infected keratinocytes. The surrounding dermis is relatively unremarkable. Intact lesions show little or no inflammatory change.

TTT

1. Benign – Neglect → self limiting
2. Physical Methods:
   - Curettage
   - Manual extract
   - Cryo
   - Electro.
3. Topical:
   - KOH (lo.)
   - TCA
   - Tretinoin
   - Aldara
   - Podophyllotoxin
   - Cantharidin.

Hand-foot & mouth dis (2014) (HFMD)

Oral vesicular disorders caused by picornavirus (RNA) (Echo, Entero V.):
(i). HFMD
(ii). Herpangina
(iii). FMD

· Causative virus (Enterovirus)
Entero → (i). Coxsackievirus A16 → most common
(ii). Cox. A6 → severe affect (vesiculobullous) extend (face, perioral, limbs, eczema coxsackium)
(iii). Enterovirus (EV-71) → sepsis (neuro-complicat-)

· Mode of Transmission (
(i) Fecal-oral route
(ii) Contact c̄ infected skin lesions or oral secretions.
(3) droplet.

· C/P: · Age < 10 y. (95% < 5 y.)
· prodroma: FAHM, sore throat & ± diarrhea.
· Rash: Tender/painful macules & vesicles on erythematous base at buccal mucosa, palate, pharynx → Hands & Feet (palm & dorsal aspects) → Erosion & ulcerat- · 1 w → resolut-
- Other area (leg, buttock, genital)

· Other features:
1. onychomadesis
2. Neurological complicat- (c̄ EV-71)

· Inv. (Ø is mainly clinical):
(i). leukocytosis, lymphocytosis, ↑CRP & ESR
(ii) Viral Isolat-: Culture, Immunoassay & PCR (detect EV-71)

· Tx → supportive measures
. Antipyretic
. Analgesic
. IV-fluid
. Amantadine & Ribavirin ??

NB ① one Hand & 2 Feet Synd → Fungal inf.
② Hand-foot Synd: pp. Erythema Induced by chemo Tx (DNNZ)
3. Foot & Mouth dis: serious, Epidemic, rare in human, Contact c̄ infected "stock" · 1 w

Gianotti-Crosti syndrome

(PAC: Papular Acrodermatitis of Childhood)

· Causative virus (1) HBV (ayw strain), EBV, Entero (Coxsackie A16), Echovirus, RSV
HBV, EBV & vaccine
(2) Bact. - Bartonella & Mycoplasma, strept.
(3) Vaccinat-

Age: 2 - 6 years. (6 ms - 12 y)

Clinically
1. Non-pruritic erythematous (dull-red, flat topped) papules (or pap. vesic) on face, buttocks and limbs lasting about (3-8) weeks. Fading with desquamation.
2. Enlargement of inguinal or axillary lymph nodes. (L.N), HSM, fever, ±dark
3. Acute hepatitis lasting for 2 months.

. Extensor
. Buttocks
. Face
. Spare
. Trunk
. Elbow
. Knee
. PP
Severe affect- is against Ø.

· Diagnosis · HBS Ag.
· Tx → Conservative.

Cutaneous manifestations of hepatitis B &/or C infection (see also p. 19 in "Dermatology & Internal Medicine")
• Mixed essential cryoglobulinemia.
• Cutaneous small vessel vasculitis.
• Urticarial vasculitis.
• Porphyria cutanea tarda.
• Polyarteritis nodsa.
• Lichen planus.
• Serum sickness-like syndrome.
• Gianotti-Crosti syndrome.
• Pruritus.
• Erythema nodosum.
• Erythema multiforme.

HL

Exanthema : Rash that occurs as a sign of systemic dis.

Viral exanthems

Definition

Any skin rash associated with a viral infection is called an *exanthema*. If the rash occurs on mucosal surfaces, it is termed an *enanthem*.

Causative viruses

The most frequently seen viral exantherns are those caused by: enteroviruses, measles, varicella, herpes simplex and parvovirus B19.

The virus disseminates to the skin through the blood during a viremic phase of the viral illness. The exanthema observed is the result of the local cutaneous host response to the virus.

• Most viruses produce similar rashes → So I Term → Non Specific Viral Rash.

Clinical types of viral exanthems and their causative viruses

1. *Widespread macular and papular eruptions (morbilliform eruptions):* Measles, rubella, HHV-6 (roseola), infectious mononucleosis (Epstein-Barr virus & cytomegalovirus) and enteroviruses.
2. *Acral-located papules (popular acrodermatitis):* affecting the fingers, toes, hands, feet, ears, nose and buttocks. Some viral infections preferentially locate to acral areas, including those that produce *the Gianotti-Crosti syndrome or papular acrodermatitis.* These viruses include hepatitis B, cytomegalovirus, Epstein-Barr virus and coxsackievirus A16.
3. *Blistering eruptions on a red base* (dew drops on a rose petal): Varicella, herpes simplex, herpes zoster and coxsackieviruses (hand, foot & mouth syndrome).
4. *A widespread lacy ,ed eruption* is characteristic of erythema infectiosum: Parvovirus B19. ↳ Reticulated
5. *Diffuse redness that mimics scarlet fever:* enteroviruses, adenoviruses and hepatitis B and C.

- HBV
- EBV
- CMV
- Cox.

Lacy

Diffuse

Differential diagnosis of morbilliform eruptions

Viral / Drug → Exanthema

→ Exanthematous DE.

Common viruses	less Common viruses	Drug eruptions 4
Measles	• Enteroviruses	Ampicillin
Rubella	• Enterovirus	Penicillin
Roseola	• Coxsackie-virus	Nonsteroidal anti-inflammatory drugs
Erythema infectiosum	• Echovirus	Salicylic acid
Pityriasis rosea	• Respiratory Vi	Barbiturates
2. Common Bacteria	• Rhino v.	Phenytoins
Scarlet fever, SSSS, TSS	• Adeno V.	Phenothiazines
[Meningococcal dis.	• RSV	Thiazide diuretics
3. Reactive erythemas	• influenza & para.	Isoniazid
Urticaria	• Parvovirus 19	Papulosquamous disorders 5.
Papular urticaria	• HHV: 4, 6, 7.	Guttate psoriasis
Erythema multiforme		Graft-versus-host disease (GVHD)

Itchy Drug

X Fever Viral

X MM

Traditonal Numbering of original 6 Exanthematous illness!

- 1st dis → Measles
- 2nd → Scarlet fever
- 3rd → German Measles
- 4th → Duke's dis. (Scarlatinella)
- 5th → Erythema Infectiosum
- 6th → Exanthema subitum

STAR Complex = Sore throat Arthri Rash.

• Guidelines for Diagnosis of Exanthemas (Morbilliform)

• Trying to detect the causative virus:

- Summer Exanthema
  - usually Enteroviruses.
- Winter Exanthema
  - usually Respiratory Viruses.

• Exanthema Acc. to the age: (جوه جدا كلينيكال)

- Children
  - usually Viral
  - " Non Itchy
- Adults
  - usually Drug
  - " Itchy

• The Three main group of Viruses are

- Enteroviruses
- Respiratory Viruses
- Human Herpes Virus gp. : HHV 4, 6, 7
  - 4 → EBV
  - 6, 7 → Roseola
- Parvovirus 19

• Discussion of some diseases caused by Viruses:

• Parvo Virus 19 can cause:

(1) Erythema infectiosum (5th d/s)

- ± ass. ē Erythema elsewhere & oral ulcers.

(2) Papular purpuric gloves & Socks Synd

- Teenagers – Young Adult
- Erythema, oedema & Pruritus ʒ Hands & feet ē sharp cut off at wrist & ankles → become purpuric

(3) Pregnancy

- Miscarriage
- Still birth
- Self limited anemia & Hydrops Fetalis.

Characteristics of

Exanth قبل
1. Fever
1. Exanth.

"Exanthema Subitum"

Erythema Infectiosum (5th dis) (Slapped cheek dis).

- Parvovirus 19, droplet & Vertical Transmission.
- 3 Stages:
  - * 1st → Slapped cheeks: asymmet Erythema affect cheeks & spare → Eyelid, → Chin
  - * 2nd → after (1–4 ds), Reticulated, Lacy erythema of Trunk & ext.
  - * 3rd (1–3 ws) → no eruption, but only recur on Hot bathing, Sunlight & Exercise.

شبه الشبكة

- * No MM

Commmest Exanthema in Age <2ys

Roseola infantum (6th dis)

- IP: 1-2 ws
- HHV 6 & 7
- Age: < 3 ys (peak at 6 ms) & if affect adult it will be IM like or Hepatitis like.
- *. Rash begins with drop of fever (3-5 d).

MM

Exanthema < 2 ys → ?? شخص بي طول

Complications: Seizures & Consciou
Enanthema: eryth. macules at soft Palate, 2 ds before Exanth.

Characteristics of

Measles (Rubeola)

- Paramyxo Virus.
- Age: < 15 ms
- IP: 9-12 ds
- prodromal (with prominent URT manif.) → Exanth. (macular or Morbilliform) at ant scalp & post auricular. —2 ds→ Spread.
- Kopliks Spots: Rash جرز

Post (cervical, occipital, auricular) LN

Cluster Ø
- High fever
- Kopliks spot
- CHIC conjunctivitis
- URT

↑ Manifest
↓ Clo

German Measles (Rubella)

Milder dis < Rubeola.

نأخر ظاهر

- Toga virus
- IP: 1-3 ws.
- Prodroma: FAHM & CHIC pain on Lat & upward Eye movem.
- Rash: smaller < Rubeola
- Forchheimer's sign: Pinhead-sized macules & Petichae on soft palate & uvula

↓ Manifest
↑ Clo

	Measles (Rubeola)	German Measles (Rubella)
· Virus	· Paramyxovirus (RNA)	Toga virus · (RNA)
· IP	· 2-3 ws ·	1-2 ws
· Infectivity period ·	· 5 ds before to 5 ds after rash	· 2 ds before & 4 ds after
· Prodroma	· Fever, Cough, Coryza, Conjunchivitis	· Children: mild - Absent · Adult: FAHM, Nusea, Pain at flat. region of head Painful. occipital L.N
· Enanthema	· Koplik's Spots: grayish-white papules at erythe. background buccal mucosa "2ds" before & 2ds after rash.	· Forsheimers Spots: Petichae on Hard palate & Soft palate (Petichae → palate)
· Exanthema	· Maculopapular rash, starts Postauricular & at Ant. Hair lines 3ds → Spread to all over the body 5d	· Maculopapular rash starts & spread Caudally from face to all over the body 1-3d · Rash is absent in 40%
· Complications	· OM, pneumonia · Encephalitis · Panencephalitis (SSPE)	· Arthritis, Encephalitis, Thrombocytopenia & Cong. Rubell Inf. (if 1st Trimester) [Cataract, deafness, CHD, Anemia, Thrombocytopenia & Muffin baby Synd "blue-Berry"]
Mx	(i). vaccinate (MMR; 12-15 ws) (ii). Supportive & Vit A	(i). Vaccine (ii). Supportive

NB1: Unilat Laterothoracic Exanth. (Asymm. periflexural Exanth. of childhood)

- Etiology ??
- prodroma (URT & GIT) → unilat. morbilliform or Eczematous rash that starts unilat (Axillae > Trunk > thigh) → spread to ! Controlat. Sites 3-8w: spont. Resolut-

NB2: · Enteroviruses (RNA, Coxsackievirus, Echo, Feco-oral & droplet):

- HFMD & FMD
- Herpangina
- Eczema Coxsackium
- Int. organs: RT, CNS, GIT.

Pityriasis rosea

(PR)

An acute, self-limiting, papulosquamous eruption with a duration of 6-8 weeks.

Pathophysiology...??

- Viral: PR has often been considered to be a viral exanthem, a view supported by the condition's seasonal occurrence, its clinical course, the possibility of epidemic occurrence, the presence of occasional prodromal symptoms, and the low rate of recurrence upper tract respiratory infections (old speaking was regarding HHV6,7, and Picronavirus...but no evidence auggested).
- Drugs : drug induced PR.

Clinical presentation: A single scaling patch (the herald patch) appears 1-60 days before the general rash. It is an oval pink or red plaque 2-5 cm in diameter, with a scale trailing just inside the edge of the lesion. The herald patch is often mistaken as ringworm. It can also be confused with psoriasis.

A few days later, more scaly patches (flat lesions) or plaques (thickened lesions) appear on the chest and back. A few may also appear on the thighs, upper arms and neck but they are uncommon on the face or scalp. These secondary lesions tend to be smaller than the herald patch. They are oval in shape with a dry surface. Like the herald patch, they may have an inner circlet of scaling. These lesions follow the relaxed skin tension lines (Langers lines) on both sides of the upper trunk so that the rash has been described as looking like a fir tree or "Christmas tree".

PR is usually asymptomatic but may be itchy . In white skin the patches are pink or red, but in darker skin they may be pigmented or they may appear white due to the scale. Postinflammatory hypo/hyperpigm. May occur.

- Recurrence : 2% but : Relapse of fading Eruptn ± occur.

Clinical varieties:

- Abortive PR: herald patch only, no 2ry eruptions.
- Inverted PR: affect acral areas (face, palmoplantar...DD; $).
- Localised: cervicofacial or girdle (axillae and groin).
- Generalized .
- Segmental, unilateral and Blaschkoid
- Short course (1-2ds) & persistent PR (ms-ys, often drug induced).

- Multiple Herald Patches. or No Herald Patch (2ry)
- Giant PR of vidal (pit.Circinata et marginata of vidal, limb-girdle PR): A morphologic variant characterized by atypical large patches that tend to be fewer in number and coalescent has been described. In this variant, commonly referred to as pityriasis circinata et marginata of Vidal or, the eruption generally appears in the axillae, the groin, or both, with the trunk and extremities usually spared.[32] Individual patches are 3-6 cm in diameter, exhibiting the characteristic central clearing and collarette of scale with surrounding erythema.

- Few
- large
- persistent
- Localized b... but ± generaliz...
- DD. T.Circinata

- Variations in the lesions: papular, vesicular, pustular, bullous, purpuric, urticarial, EM like, lichenoid, photoexacerbated, oral, vulval and penile.

DD:

- *2ry syphilis:* no herald patch, palmoplantar predilection, generalized LN, other manifestations, serology.
- *Pityriasiform drug eruption* (ACEI, ketotifen, bisthmus, gold, barbiturates): no herald patch, marked itching, lichenoid rash, prolonged course, postinflamm. Pigm.
- *Pityriasiform SD:* no herald patch, at midline trunk, other seborrheic areas. & Scalp, dull in Color, Thick Scales
- *Others:* guttate Ps.& T. corporis.

NB: PR in 1st Trimester ± → Abort± or premature

Treatment

1. Reassurance (PPR): → self limiting.
2. Symptomatic th: Antihistamines & Topical Cs
3. Erythromycin: 250 mg X 4 /d X 2 wk (Earlier initiat → ± Complete Clearance)
4. NB-UVB: ↓ severity but ± → Hyperpigm.
5. Systemic Cs & Dapsone: For wide spread & Eczematous PR
6. "Acv":

EBV

1ry Inf. (IM) = "glandular Fever" → Latency → Reactivate

- IP: 1- 30 days.
- prodroma < 0 Sympt. in children
  Sympt. Adolescent & young Adults. (FAHM)
- Clp (80%): Fever, L.N, Pharyngitis, Others
- Rash: Morbilliform or Non specific ≠ Vasc purpura
- Splenomegaly
- Tonsillitis & Hepatitis
- Lymphocytosis & Atypical lymphocytes.
- ± Petichae < eyelid, palate, cut.

Monospot Test ←

Serology: Heterophil anti EBV Abs that react é: (1) Sheep RBCs (Paul Bunnel test) (2) Horse " (Monospot test)

- in B-lymphocytes

Latency → Reactivate

Tm: BCL, Burkitt lymphoma, Naso pharyngeal carcinoma

- oral Hairy leukoplakia
- Hydroa Vacciniforme
- Necrotic Hypersensitivity to Mosquitoes Bites.
- Gianotti Crosti

Cutaneous of EBV

- Morbilliform
- Urticaria
- UV
- EM & EN
- PAC
- CBDC
- PLC
- Hairy leukop.
- Hydroa V.
- Annular Eryth.
- Reactive genital ulcers.

Complications

(1) Common: Morbilliform rash of take (Ampicillin Induced Empiric) ← Penicillin or Cephalosporin (Not true reactivity → Safe drugs)

(2) Rare: purpura, pancytopenia, encephalitis ...

CMV

1ry Inf. → Latency → Reactivate

Latency:
- monocytes.
- macrophages.

(1) Immunocompetent (IM like)
- IP: 1-2 m.
- Clp: Im like but..
  - less severe
  - No Tonsillitis.
  - No Heterophile Ab.
  - 33% morbilliform or petichiae.

(2) Cong & Neonatal (5-10%) ← IUGR, Jaundice, Thrombocytopenia, Chorioretinitis, Blue-berry muffin baby

(3) AIDs: Esophagitis, Colitis, Pneumonitis, Chorioretinitis.

Reactivate:
- Usually in Immunocompromised
- See 1ry inf.
- In AIDs & Immunocomp.

Antiviral:
- Ganciclovir
- Valganciclovir
- Cidofovir
- Foscarnet

HHV6

1ry Inf.

(6th dis) (1) Ac Scala Infantum (Exanthema Subitum)

Wic · 6mo - 2y

· 3-5 ds fever → drop → rash

Cut: Rose-red macules or papules ± surr by white Halo

MM: Nagayama's Spots: red papules on soft palate

· ± Palpebral Edema / Febrile Seizures

(2) IMN Like in Adult.

(3) Febrile Synd. without Cut. Empl=

Reactivat=

· DRESS

· PR.

Periorbital Edema

(1) Bilat.
- ACD
- Cellulitis
- Kawasaki
- Trichinosis

(2) unilat.
- Insect bite
- Chagas dis
- Thyrotoxicosis
- unilat Conjct.
- Retroorbital TM.

(3) in ER: Hagland Sign (Bilat. Eyelid Edema).

HHV7

1ry Inf.

(1). Usually Asympt.,
1st 5y of life.

(2). (±) Roseola Infantum.
(less common than HHV6)

(3). ± Febrile Seizures / Acute Hemiplegia.

Reactivat=

· DRESS

· PR.

Fever + Skin Rash.

Infect | **Inflamm.** | **Others.**

A. **Bact:**
- TSS
- SSSS
- Scarlet fever
- Septic emboli → Rickettsia, meningococcemia
- & & ECM

B. **Viral**
- Enteroviruses
- Adenoviruses
- HHV6
- VZV
- HIV

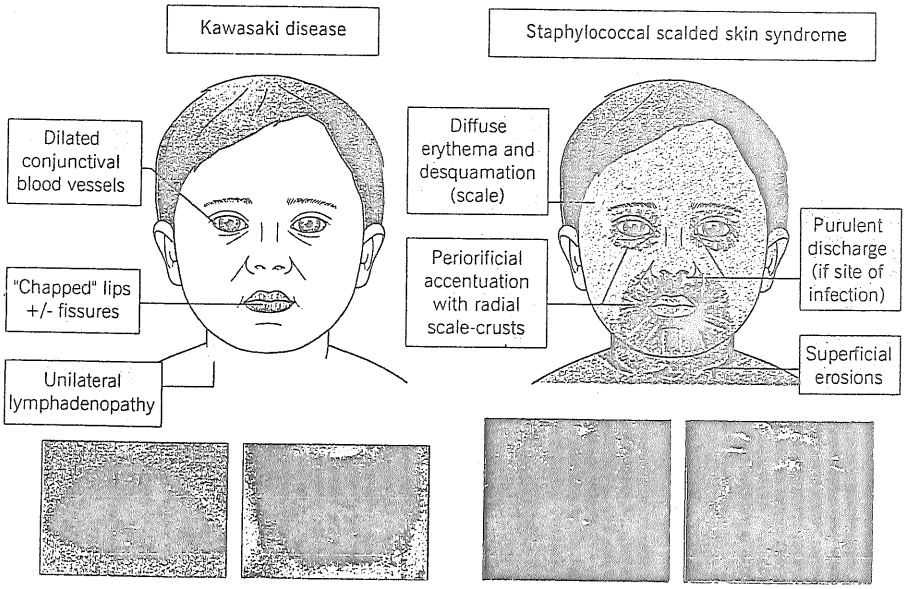
C. **Fungal:** Systemic Mycos

D. **Protozoa.** Strongyloidiasis.

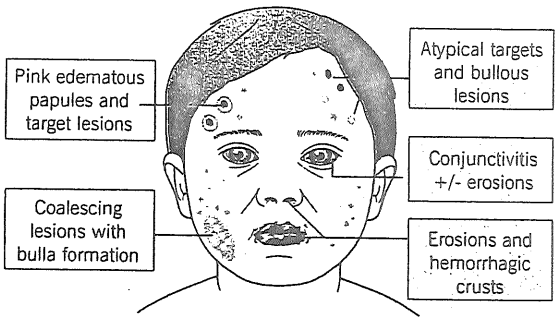
Inflamm.
- GVHD
- DRESS
- AGEP
- SJS/TEN
- EM
- Serum sickness like Reacⁿ
- AICTDs

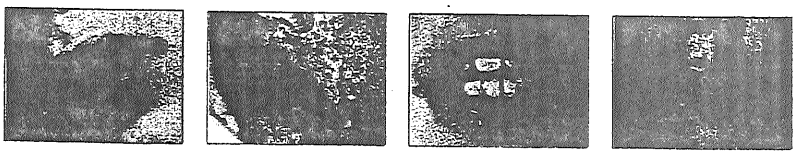
Others.
- Kawasaki
- periodic fever Synd.
- Lymphoma..

FACIAL FINDINGS IN KAWASAKI DISEASE, STAPHYLOCOCCAL SCALDED SKIN SYNDROME AND ERYTHEMA MULTIFORME MAJOR/STEVENS-JOHNSON SYNDROME



Erythema multiforme major/Stevens–Johnson syndrome





Severe Cut. Adverse React= (SCAR)

- DRESS
- SJS/TEN
- AGEP
- Drug induced Erythroderma

DRESS = DHS (drug Hypersensitivity Synd) → (or Anticonvulsant HS)

Drug intake "Anticonvulsant"

- Most Common: Aromatic Anticonvulsants:
  - Carbamazepine
  - phenytoin
  - phenobarbital
- · Antiepileptics · Allopurinol · Sulfonamides → أهم ٣
- Others: Sulfa, Allopurinol, Azath., Dapsone, Terbinafine.

Onset:
- أول مرة أخذ الدواء (2 - 8 Ws) فترة طويلة مقارنة بالأنواع الأخرى من DE
- ثاني مرة كمان → 1 day.

↓

- Fever
- Rash
- L.N
- Pharyngitis
- Facial oedema

· Rash (90%):
- Most Common: Morbilliform (90%)
- Others: Erythrodermic, Urticarial, Bullous (SJS/TEN like; but Not d.t. KCs necrosis but d.t. Cut. Edema); Pustular; Targetoid.

· L.N (75%): Painful either: local Cervical or Generalized.

· Pharyngitis (25%): pharyngeal, oral, labial ulcerat= or Strawberry Tongue (± genital).

Facial Oedema (30%) (or Angioedema) → DE مساعد هام للتشخيص لأن الأنواع الأخرى لا تؤثر على الوجه.
- Sign of Severe systemic affect=.

↓

Int. organ affect= Sp.
- Liver
- Blood
- Kidney
- others

(MR 20-40%)

· Hepatitis (70-90%): ↑enzs, ± fulminant.

· Blood (50%): Leucocytosis ē: Eosinophilia (80%), Neutrophilia, Atypical lymphocytosis.
- Anemia & thrombocytop.

· Others: Nephritis, Carditis, Pneumonitis, Myositis, GIT, Encephalitis, Thyroiditis.

Criteria of diagnosis of DRESS

1- The European Registry of Severe Cutaneous Adverse Reactions to Drugs and Collection of Biological Samples **(RegiSCAR)** :require at least 3 of the following:

- Hospitalisation
- Reaction suspected to be drug related
- Acute skin rash
- Fever about 38 Celsius
- Enlarged lymph nodes at two sites (≥ 2)
- Involvement of at least one internal organ (≥ 2)
- Blood count abnormalities such as low platelets, raised eosinophils or abnormal lymphocyte count.

↑WBCs ↑Eos.

2. Japanes Criteria: (7 = Typical DRESS; 5 = Atypical DRESS.)

- Maculopapular Rash develops ≥ 3 ws after drug.
- Prolonged clinical symptoms ≥ 2 after stop ".

other: · Facial Edema · pharyngitis

- Fever $> 38\,^{\circ}C$
- L.N
- Leukocytic Abnormalities → leukocytosis (> 11000); Eosinophilia (> 1500); Atypical lymphocytosis ($> 5\%$)
- SGPT > 100 U/L.
- HHV6

Diagnosis

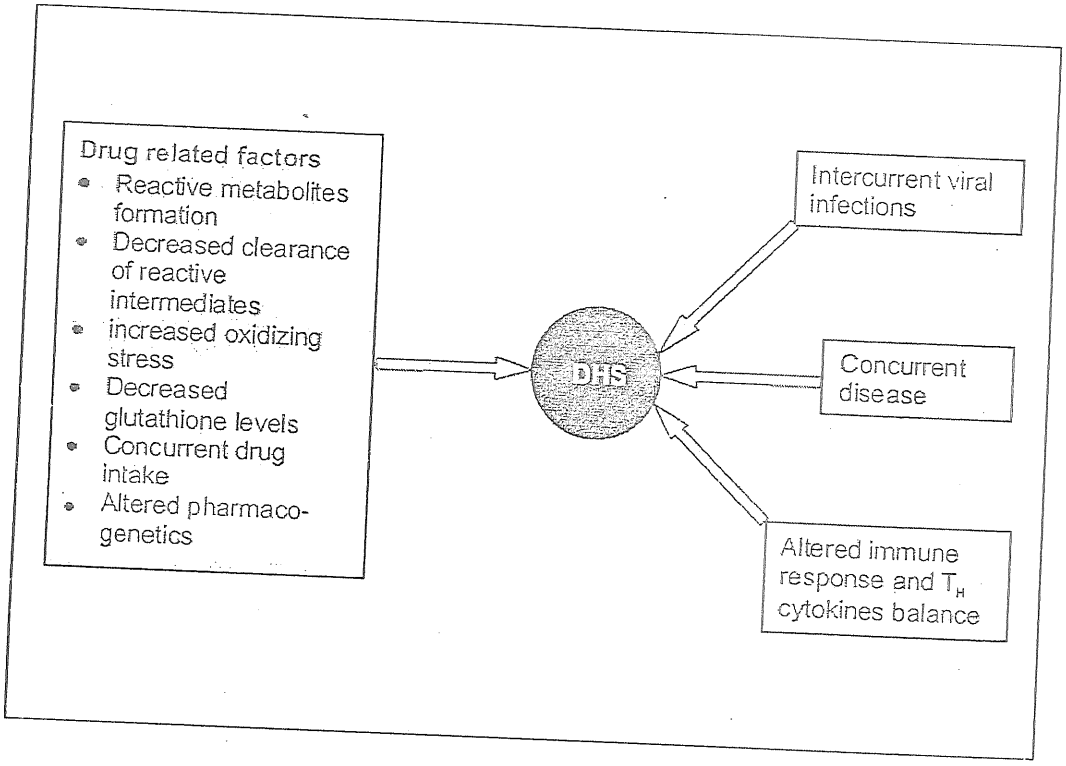
(i) HP
- Perivascular infill. < dense superficial
- Spongiotic or lichenoid dermatitis
- Dermal Edema
- LN: Pseudolymphoma like ē Atypical cells.

(ii) Lymphocytes Toxicity Assay
نقيس تأثير الدواء على WBCs مريض

Patch testing
صعب مايكون شغال
- 50% +ve ē Anticonvuls.
- But -ve ē Allopurinol.

Diagnosis	Rash	Onset	Fever	Internal organs	Arthralgia	Lymphadenopathy
DHS/DRESS	Exanthematous, Exfoliative dermatitis, Urticarial plaques, Pustular eruption, SJS-TEN	1-8 weeks	Present	Present	Absent	Present
Pseudolymphoma	Single or multiple nodules	6 months	Absent	Absent	Absent	Present (biopsy shows atypical hyperplasia simulating malignancy)
Serum sickness–like reaction	Urticarial, Exanthematous	7-14 days	Present	Absent	Present	Present

ETIOPATHOGENESIS



TTT

A. **Patients with non–life-threatening or non–organ-threatening disease**

Discontinue anticonvulsant

Supportive therapy (e.g., antihistamines, topical corticosteroids)

Obtain complete blood count, carry out liver function tests, urinalysis, serum creatinine, baseline thyroid function tests, other tests based on symptom presentation

Skin biopsy, if blistering or pustular eruption

Advise patient regarding potential for cross-reactivity

Counsel family members and first-degree relatives regarding increased risk

Advise patient to obtain a MedicAlert

B. **Patients with life-threatening or organ-threatening disease**

All the above measures *plus*

Use of oral prednisone or pulse methylprednisolone

Intravenous immunoglobulin and cyclosporine can be used as alternatives or adjuvants

Vaccines in Dermatology

- HPV → موجود قبل كده

TB

(1). BCG (Bacillus Calmette G.)

(2). live attenuated (LAV)

الجرعة: اول حقنة بالجلد بعد الولادة أو بعدذلك لو هم عيزه خطر العدوى

استعمالات أخرى: حساسية لمادة في حالات السل وسرطان المثانة

Leprosy

(1). BCG (ConVit)

(2). BCG + Killed M. leprae

(3). Tawalars (M. Welchii strain)

(4). Subunit Vaccine.

بعطى لاى حد معرض للعدوى.
أو عايش في منطقة Endemic.

HSV (under trial)

- Killed whole Vaccine
- LAV
- Recombinant Glycosylated subunit.

اى حد معرض للعدوى .. بالذهاب إلى هو Sero + وجوزها Sero -Ve

Varicella

طبعا مفروض..

(1). Varivax] LAV

(2). MMR-V

بعطى عند سن ١٢ - ١٥ شهر.
وبكرر عند ٤-٦ سنوات.

- Prevent infection or Severe attacks
- ↓ incid. of PHN

HBV

- Subunit.
- Recombinant.

* 3 IM doses at: 0, 1, 6 m.

اى حد بتعامل مع دم أو معرض للعدوى زى الغسيل الكلوى

HIV (under trial)

- AIDS-VAX : gp120 subunit.
- Subunit
- Recombinant

اى حد معرض للعدوى (طبعا معروفين) ليه صعب وتصنيعه بدأ كليتيه نظرى في كتاب STDs.

MMR

- LAV
- Dose: as Varicella

Acne

- "Component Vaccine"
- "Inactivated" whole Bact.

بيشتغل ازاي

↓ IL8 & MIP2 (macrophage Inflammatory protein) Released By P. Acnes.

Melanoma

- Whole Cell Tm Vaccines
  - Autologous Tm Vaccine
  - Allogenic " "
  - Peptide Vaccines
  - Ganglioside "
- Idicats: Metastatic Melanoma.

يحقن عضل أو تحت الجلد أو بالجلد

في أي Limb بيعمل إزالة لل MM

- "HPV"
- "Leishmania"

HPV Vaccines

Why HPV is dangerous?	-HPV is Highly oncogenic.. Virtually all cases of cervical cancer, 95%cases of anal cancer &70 % of oropharyngeal cancers are due to HPV. - Dozen high-risk HPV types have been identified. Two of these, HPV types 16 and 18 (16>>18). -HPV 6&11 are responsible for 90%of genital warts. - CDC :estimates that more than 90 % and 80 %, respectively, of sexually active men and women will be infected with at least one type of HPV at some point in their lives . Around 50% are with a high-risk HPV type. - Most high-risk HPV infections occur without any symptoms, go away within 1 to 2 years, and do not cause cancer. Some HPV infections, however, can persist for many years. Persistent infections with high-risk HPV types can lead to cell changes that, if untreated, may progress to cancer.
Mechanism	- HPV vaccines are based on virus-like particles (VLPs) that are formed by HPV surface components (Major capsid protein L1). (Purified protein prod.) ∴ - VLPs are not infectious, because they lack the virus's DNA. However, they closely resemble the natural virus, and antibodies against the VLPs also have activity against the natural virus
Types	- Cervarix or bivalent vaccine: (HPV:16,18): FDA (2009) - Gardasil 4 or quadrivalent vaccine: (HPV:6,11,16,18): FDA (2006 In females&2009 in males) - Gardasil 9 or nonavalent vaccine : (as G4+HPV 31, 33, 45, 52, and 58): FDA (2014).

(Attenuated)	Killed	Purified
. Measles . Mumps . Rubella . BCG . VZV	. Typhoid . Rabies . Cholera . HAV	. HPV . HBV . Diphtheria . Tetanus .

Indications	The Advisory Committee on Immunization Practices (ACIP), recommendations: - Initiation at age 11-12 years (but can be at 9 years) - Females aged 13 -26 years and males aged 13-21 years who have not been vaccinated previously or who have not completed the three-dose vaccination series. - Males aged 22 through 26 years may be vaccinated. - Vaccination through age 26 years of men who have sex with men and for immunocompromised persons if not vaccinated previously
Dose (IM)	- WHO: two doses, 6 months apart - US: 3 doses at 0, 2, and 6 months
Efficacy	- Gardasil and Cervarix: provide nearly 100 % protection against persistent cervical infections with HPV types 16 and 18 and the precancerous cervical cell changes - Gardasil 9: is effective as Gardasil as regard HPV4 Types, and 97 % effective in preventing cervical, vulvar, and vaginal disease caused by the five additional HPV types (31, 33, 45, 52, and 58).
Duration of protection	Gardasil for 8ys, Cervarix for 9ys
Efficacy	- Gardasil and Cervarix: provide nearly 100 % protection against persistent cervical infections with HPV types 16 and 18 and the precancerous cervical cell changes - Gardasil 9: is effective as Gardasil as regard HPV4 Types, and 97 % effective in preventing cervical, vulvar, and vaginal disease caused by the five additional HPV types (31, 33, 45, 52, and 58) that it targets
When to start sex after vaccination?	Sex should be avoided till completion of the 2 or 3doses (after 6ms)
Can we give them in already infected persons?	- HPV vaccines are safe when given to people who are already infected with HPV, the vaccines do not treat infection. They provide maximum benefit if a person receives them before he or she is sexually active. - It is likely that someone exposed to HPV will still get some residual benefit from vaccination, even if he or she has already been infected with one or more of the HPV types included in the vaccines.

	- At present, there is no generally available test to show whether an individual has been exposed to HPV. The currently approved HPV tests show only whether a person has a current infection with a high-risk HPV type at the cervix and do not provide information on past infections.
Can we give them in those having cervical cell changes?	- Yes , should still receive HPV vaccination if they are in the appropriate age group because the vaccine may protect them against high-risk HPV types that they have not yet acquired. – Neither treat the already HPV inf. Nor the abnormal Pap test
After vaccination, is Pap smear still important?	Yes. Because these vaccines do not protect against all HPV types that can cause cancer, screening continues to be essential to detect precancerous changes in cervical cells before they develop into cancer. In addition, cervical screening tests—HPV DNA test alone, or HPV and Pap test together, also known as co-testing—are critically important for women who have not been vaccinated or who are already infected with HPV.
Adverse effects	- Most were minor and not greater than background rates compared with other vaccines, the exception being higher rates for syncope (is it from injection or vaccine..???any way; Patients should remain seated for 15 minutes after injection) and **thromboembolism** (0.2cases/100.000). - Other adverse events include local site reactions, headaches, hypersensitivity reactions, and urticaria.
Does Gardasil Increase Risk of Precancerous Lesions, or Worse?	- According to information the manufacturer of this vaccine presented to the FDA prior to approval, if a person has already been exposed to HPV 16 or 18 prior to injection Gardasil increases the risk of precancerous lesions, or worse by 44.6%. - Is this information advertised? No! This information was actually presented to the FDA by Merck. It came from their own safety trials. The FDA did not respond by recommending screening for HPV prior to vaccination. The FDA did not even demand a warning be included in the package insert. - Now, Merck's research is indicating that Gardasil may also "provide cross-protection" against other strains of HPV that are closely related to HPV 16 and 18. (see this article on Medpage Today) This means prior exposure to these additional strains may pose an increased risk for cervical cancer also, if combined with vaccination - No one appears to be concerned with the increased risk of vaccination combined with prior exposure, as long as you take the vaccine. You will see no advertisements indicating the possibility of increased risk of the very cancer this vaccine is supposed to help you avoid.
Price	$130 to $160 per dose

نقاط مهمة (ملخص)

(1). HPV
- 100% Cancer Cx
- 95% " anus
- 70 oropharyngeal.

(2). Vaccine : purified product Major Capsid protein L_1 توضيح

(3). Efficacy
- persistent Inf (100%)
- precancerous & cancerous lesions of C.Cx (97-100%)
- Vulvar & Vaginal Cancer (Gard.)

(4). ممنوع معا شرة الا بعد ٣ جرعات (WHO (جرعتين فقط))

(5). (Inf. نعطيه لمصابة)
- لا يعالج.
- pap. لا يغير.
- لو اتعدت

نعطيه لو عندها عدوى لسببين
1. Residual effect ±
2. protect by others types who haven't catched by the pt.; also cross activity

(6). نتيجته تمتد لفترة ٨-٩ سنوات

(7). S.E :
- Local: pain, Erythema, Swelling, pruritus, urticaria
- Syncope
- Thromboembolism.

Cervarix (2)	Gardasil (4)
No protect against genital warts 16, 18	protect.
0.5ml, IM: 0, 1, 6ms	0, 2, 6 m.
Age approval: ♀ 10-25y	♀: 9-26 ♂: 9-15
Catch-up: 8-25 y	8-26 y
Elderly: ♀ 26-55	Not recommended for ♀ > 26
~~Cross protect: HPV 31 & 45~~	